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SURGERY

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Original Communications

THE EFFECT OF ADRENAL CORTICAL HORMONES IN HEMORRHAGE AND SHOCK*

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IN A NUMBER of recent publications¹⁻⁴ a favorable influence on secondary shock has been claimed for the adrenal cortical hormones. In our view the validity of such claims can be judged best in terms of the ability of these hormones to correct a quantitative deficiency in the volume of circulating plasma, as this is the most characteristic objective feature of shock. Although measurements of plasma volume may not be valid during the actual state of shock, information of value in this respect is obtainable during hemorrhage before the onset of shock and while plasma volume determinations are still reliable. The purpose of this communication is to report our observations on the effect of the adrenal cortical hormones, first, on the circulating plasma volume in hemorrhage before the onset of shock, and second, on the blood pressure curve and survival time following the onset of shock due to hemorrhage.

THE INFLUENCE OF ADRENAL CORTICAL HORMONES ON THE CIRCULATING PLASMA VOLUME AND PLASMA PROTEIN IN HEMORRHAGE

1. *Massive Hemorrhage Without Producing Shock.*—The volume of circulating plasma and the total plasma protein of normal unanesthetized dogs, deprived of food, but not water, for the preceding twenty-four hours was determined by the Evans' blue dye and specific gravity methods respectively.^{5, 6} They then were bled over a period of ten to twenty minutes (by needle puncture of the jugular vein or the femoral artery) of some 30 to 40 per cent of their estimated† blood volume.

*The expenses of this investigation were defrayed in part by the Proctor Fund, Harvard University.

†The figures for the original circulating plasma volume were not available until some time after the bleeding was performed.

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Shock did not result. The dogs remained active and frisked about, apparently unharmed by the massive hemorrhage. Four hours later the circulating plasma volume and total plasma protein were again determined. From these data the compensatory mobilization of fluid and protein from extravascular depots was then calculated.

Such observations were made in eight different groups of dogs as shown in the accompanying tables (Tables I and II).

A. *The Mobilization of Fluid:* Five control dogs (Group I) regained an average of 53 per cent of the plasma volume lost. Eight dogs (Group II) in which cortin* was injected intravenously immediately after the hemorrhage, in doses varying from 2 c.c. to 10 c.c. (100-500 dog units), regained an average of 67 per cent of the plasma volume lost. Four dogs (Group III) receiving 150 c.c. of physiologic saline solution distributed widely in the subcutaneous tissues immediately after the hemorrhage, regained an average of 79 per cent of the plasma volume lost. Seven dogs (Group IV) were given cortin, as in Group II, together with saline solution, as in Group III. The return of lost plasma volume to the circulation averaged 90 per cent. Four dogs (Group V) were given 150 c.c. of plasma subcutaneously, distributed widely as was the saline solution in Group III. The compensatory plasma return averaged 68 per cent. In five dogs (Group VI) which were given cortin, as in Group II, and plasma, as in Group V, the compensatory plasma return averaged 81 per cent.

From an analysis of the data in Table I† it appears that cortin does not effect a better mobilization of extravascular fluid than will occur without it. The presence of an interstitial reservoir of saline solution by itself will achieve as much. However, when cortin and saline solution are provided together, the advantage is substantial in that almost all of the lost plasma volume is replaced within the four-hour period.

Following massive hemorrhage which does not result in shock, a certain usefulness therefore may be claimed for cortin if physiologic saline solution is provided subcutaneously.

Three dogs (Group VII) which were given 10 to 15 mg. of desoxycorticosterone acetate‡ intravenously, instead of cortin, mobilized an average of 69 per cent of the plasma volume withdrawn. Five dogs (Group VIII) which received the desoxycorticosterone acetate and saline solution, as in Group III, mobilized an average of 75 per cent, which was about the same as when saline solution alone was given.

From the data in Table I it appears that desoxycorticosterone acetate exerts no significant effect on the mobilization of fluid into the blood

*Kindly furnished by The Upjohn Company as Solution of Adrenal Cortical Extract.

†The conclusions drawn in the subsequent text as to the role of the hormone in the mobilization of fluid and of protein are based on a statistical analysis of the data. Positive results are claimed only for the data in Groups IV and VI of Table I and Group VI in Table II. "p" equals 1.3, 3.1, and 2.75, respectively, in these three groups.

‡Kindly furnished by Ciba Pharmaceutical Products, Inc., under the trade name Percorten.

stream after hemorrhage which does not result in shock, whether or not an interstitial reservoir of saline solution is provided.

Three of the five control dogs (Group I) died within twenty-four hours, whereas all other animals, except one in Group IV which had been bled on a previous occasion, survived. This does not prove that the hormones possess any special virtue under the conditions of these experiments because those dogs receiving saline solution alone or plasma alone also survived.

COMMENT. One of the difficulties in a comparative evaluation of the results of different investigators arises from marked differences in the dosages of the hormones utilized. For example, Weil, Rose, and Browne³ gave rats 10 c.c. of cortin plus 10 mg. of desoxycorticosterone acetate before and 10 c.c. of cortin plus 10 mg. of desoxycorticosterone acetate after trauma. Our doses, which in proportion to body weight were only a small fraction of these, approximate effective physiologic dosages much more closely and are, therefore, more consistent with practical therapeutics. There was, however, no noticeable difference in the effect between the smallest and largest dosages which we utilized.

B. *The Mobilization of Protein*: Table II shows the average per cent of the circulating plasma protein lost by hemorrhage which was regained in the subsequent period of four hours, as follows: Group I (control), 30 per cent; Group II (cortin), 30 per cent; Group III (saline solution), 27 per cent; Group IV (cortin plus saline solution), 46 per cent; Group V (plasma), 32 per cent; Group VI (cortin plus plasma), 62 per cent; Group VII (desoxycorticosterone acetate), 24 per cent, and Group VIII (desoxycorticosterone plus saline solution), 31 per cent.

Cortin alone, therefore, seems unable to produce any favorable effect on the compensatory mobilization of lost plasma proteins. Saline solution alone likewise offers no advantage in this respect. The value of cortin plus saline solution is doubtful. But cortin plus plasma achieves an appreciable result. Desoxycorticosterone acetate is wholly ineffective, whether given alone, with saline solution or, as in one unlisted experiment, with plasma.

COMMENT. The mobilization of protein by cortin is presumably dependent, in some degree at least, on the amount of protein available in reserve depots, because the cortin was inactive until an extra supply of plasma was provided. An extra supply of saline solution or of plasma alone in the four-hour period of observation did not succeed in adding protein to the circulation.

The ratio between the amount of protein mobilized and the volume of plasma fluid mobilized varied widely in all groups (except Groups IV and VI, in which the individual ratios showed less disparity). Perhaps this is an indication of a considerable variation in the amount of plasma protein in reserve, which is to be expected among laboratory animals whose nutritional status varies widely.

TABLE I

EFFECT OF ADRENAL CORTICAL HORMONES ON PLASMA VOLUME RECOVERY FOUR HOURS AFTER MASSIVE HEMORRHAGE IN NORMAL UNANESTHETIZED DOGS

GROUP NO.	HORMONE (WITH OR WITHOUT PARENTERAL FLUID)	DOSE OF HORMONE	ORIGINAL PLASMA VOLUME WITHDRAWN (%)	LOST PLASMA VOLUME MOBILIZED (%)
I	No hormone; no parenteral fluid	-	33	52
		-	43	26
		-	37	67
		-	44	53
		-	31	65
Average				53
II	Cortin; no parenteral fluid	2 c.c.	35	88
		2 c.c.	40	44
		2 c.c.	41	66
		2 c.c.	39	55
		2 c.c.	26	43
		2 c.c.	38	77
		4 c.c.	35	96
Average				63
III	No hormone; subcutaneous saline solution	-	24	72
		-	28	120
		-	41	54
		-	33	71
Average				67
IV	Cortin and subcutaneous saline solution	2 c.c.	36	118
		2 c.c.	40	114
		2 c.c.	46	80
		10 c.c.	38	83
		10 c.c.	43	84
		10 c.c.	36	74
		10 c.c.	40	77
Average				79
V	No hormone; subcutaneous plasma	-	32	32
		-	35	80
		-	40	72
		-	39	87
Average				68
VI	Cortin and subcutaneous plasma	2 c.c.	44	126
		2 c.c.	39	49
		10 c.c.	42	91
		10 c.c.	26	45
		10 c.c.	37	96
Average				81
VII	Desoxycorticosterone acetate; no parenteral fluid	10 mg.	35	76
		15 mg.	37	54
		15 mg.	31	76
Average				69
VIII	Desoxycorticosterone acetate; subcutaneous saline solution	10 mg.	34	81
		10 mg.	35	69
		10 mg.	38	78
		15 mg.	30	45
		15 mg.	35	100
Average				75

TABLE II

EFFECT OF ADRENAL CORTICAL HORMONES ON PLASMA PROTEIN RECOVERY FOUR HOURS AFTER MASSIVE HEMORRHAGE IN NORMAL UNANESTHETIZED DOGS

GROUP NO.	HORMONE (WITH OR WITHOUT PARENTERAL FLUID)	DOSE OF HORMONE	ORIGINAL PLASMA PROTEIN WITHDRAWN (%)	LOST PLASMA PROTEIN MOBILIZED (%)
I	No hormone; no parenteral fluid	-	33	27
		-	43	26
		-	37	16
		-	44	34
		-	31	51
Average			30	
II	Cortin; no parenteral fluid	2 c.c.	35	38
		2 c.c.	40	22
		2 c.c.	41	36
		2 c.c.	39	32
		2 c.c.	26	1.7
		2 c.c.	38	39
		4 c.c.	35	50
		10 c.c.	36	21
Average			30	
III	No hormone; subcutaneous saline solution	-	24	0
		-	28	69
		-	41	21
		-	33	19
Average			27	
IV	Cortin and subcutaneous saline solution	2 c.c.	36	76
		2 c.c.	40	48
		2 c.c.	46	40
		10 c.c.	38	46
		10 c.c.	43	50
		10 c.c.	36	30
		10 c.c.	40	21
Average			46	
V	No hormone; subcutaneous plasma	-	32	5
		-	35	36
		-	40	32
		-	39	55
Average			32	
VI	Cortin and subcutaneous plasma	2 c.c.	44	100
		2 c.c.	39	27
		10 c.c.	42	67
		10 c.c.	26	48
		10 c.c.	37	69
Average			62	
VII	Desoxycorticosterone acetate; no parenteral fluid	10 mg.	35	29
		15 mg.	37	15
		15 mg.	31	28
Average			24	
VIII	Desoxycorticosterone acetate; subcutaneous saline	10 mg.	34	30
		10 mg.	35	19
		10 mg.	38	50
		15 mg.	30	14
		15 mg.	35	41
Average			31	

2. *Massive Hemorrhage Producing Shock.*—If the hormones are to be regarded as effective therapeutic agents in shock, their beneficial action should be demonstrable when hemorrhage or any other trauma has resulted in a state of shock, for in this state there is a far greater

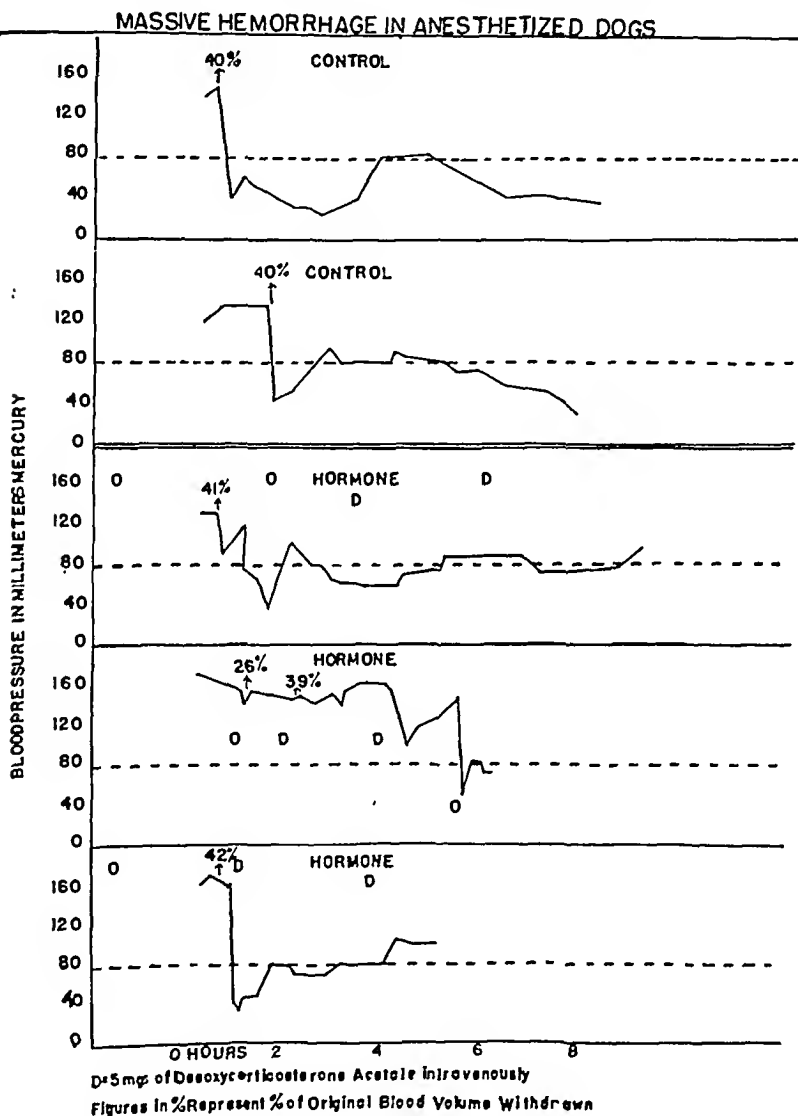


FIG. 1.

need for compensation than is the case under the conditions described in the preceding experiments. But plasma volume determinations in the shock state may not be reliable, so that a quantitative estimate of the capacity of the hormones to mobilize extravascular fluids during shock is perhaps not possible. A favorable response to the hormones

during shock can at present be assumed only if they effect a sustained return of the blood pressure level to well above the shock level and (or) a significant prolongation of the survival time.

Observations along these lines were made as follows: A group of dogs was submitted to massive hemorrhage. Heparinization and intraperitoneal nembutal anesthesia were utilized in order to record continually the blood pressure in the carotid artery. In contrast to unanesthetized dogs which survived an acute blood volume loss of some 40 per cent without going into shock, the anesthetized dogs uniformly and promptly went into shock. A systolic blood pressure level of 80 mm. Hg or lower for thirty minutes or longer was regarded as evidence of a state of shock.

Two dogs so prepared were rapidly bled of 40 per cent of their estimated blood volume. Their blood pressure curves promptly fell to shock level and death occurred in about seven hours (Fig. 1).

Three dogs treated in similar fashion were given five mg. of desoxycorticosterone acetate intravenously at intervals before and during shock as indicated in Fig. 1. This hormone exerted a slight but insignificant improvement on the course of events. Similarly, cortin given to two such dogs produced no substantial benefit.

That we were not dealing with a type of shock from which recovery was impossible and which, therefore, may have masked the possible sustaining powers of the hormones is evident in the case of five dogs, all of which recovered after being in profound shock for one-half hour or longer, following an intravenous injection of 500 c.c. of saline solution or 200 c.c. of plasma (Fig. 4 and Table III).

TABLE III

THE EFFECT OF INTRAVENOUS FLUIDS WITH AND WITHOUT CORTIN ON THE TIME NEEDED FOR RECOVERY FROM A CONSTANT SHOCK LEVEL TO A STABILIZED RECOVERY LEVEL OF BLOOD PRESSURE

EXPERIMENT NO.	INTRAVENOUS TREATMENT APPLIED 30 OR MORE MINUTES AFTER ONSET OF SHOCK	B.P. BEFORE HEMORRHAGE (MM. HG)	ORIGINAL BLOOD VOLUME WITHDRAWN (%)	STABILIZED B.P. AFTER TREATMENT (MM. HG)	TIME NEEDED TO REACH STABILIZED RECOVERY LEVEL OF B.P. FOLLOWING PER-SISTENT SHOCK LEVEL OF B.P.
1	500 c.c. saline solution intravenously	130	35	80	120 min.*
2		150	43	130	145 min.
3		155	55	118	60 min.
4	10 c.c. cortin; 500 c.c. saline solution intravenously	185	56	140	20 min.
5		140	35	100	Almost immediately
6		150	44	115	Almost immediately
7		140	50	110	Almost immediately
8	200 c.c. plasma intravenously	170	41	145	Almost immediately
9		160	45	125	185 min.
10		150	31	90	120 min.
11	10 c.c. cortin; 200 c.c. plasma intravenously	110	40	105	95 min.
12		145	18	125	216 min.

*Recovery level did not rise above 80 mm.; dog died 48 hours later.

Although cortin is without effect during shock in the absence of intravenous saline solution or plasma, it apparently possesses a slight adjuvant quality if combined with saline solution. The return of the blood pressure to a sustained recovery level occurred almost *immediately* in four out of five dogs which received 10 c.c. of cortin in addition to 500 c.c. of physiologic saline solution intravenously, in contrast to a recovery after 145 minutes, 120 minutes, and 60 minutes, respectively,

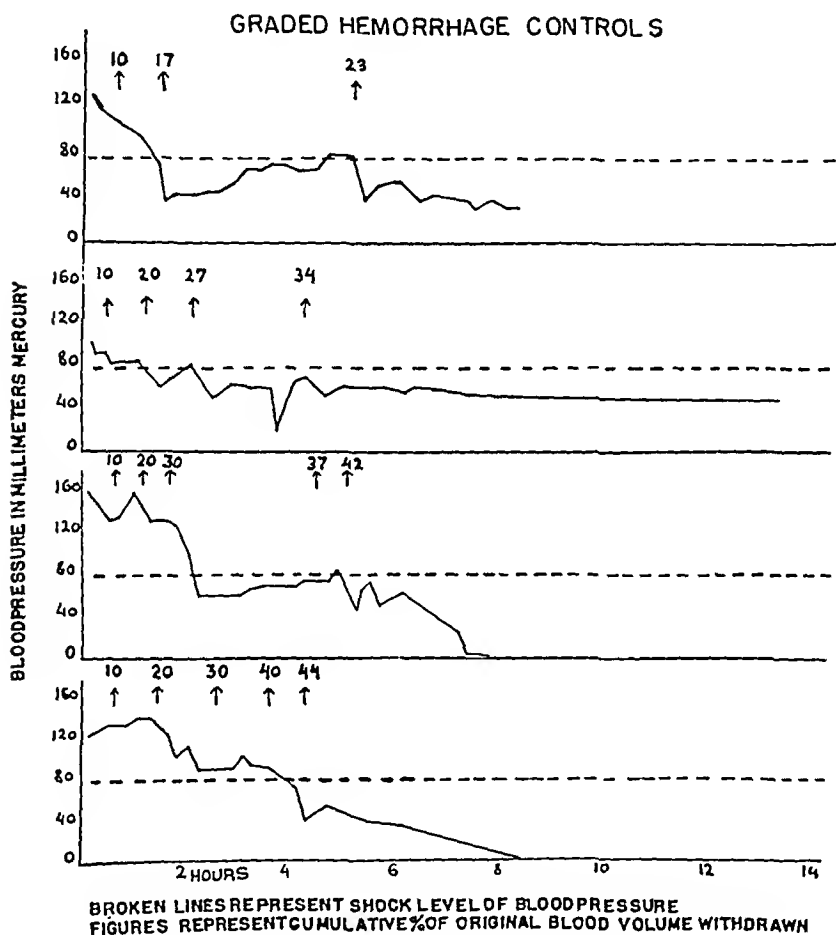


Fig. 2.

in three dogs receiving saline solution only. Plasma alone restored the blood pressure in two dogs after 185 and 120 minutes, respectively, while 10 c.c. of cortin plus plasma effected the same result after 216 and 95 minutes, respectively (Fig. 4 and Table III).

3. *Graded Hemorrhage Producing Shock.*—Since a single massive hemorrhage precipitates shock in the anesthetized dog almost immediately, it is possible that too little time is available for the organism to

benefit by whatever fluid mobilizing capacity the hormones might exert under less strenuous circumstances. Accordingly, the above experiments were repeated, substituting for a single massive hemorrhage, successive withdrawals every forty to sixty minutes, of an estimated 10 per cent of the original total blood volume so as to prolong the period preceding the onset of shock and to allow more time for the mobilization of extravascular fluids.

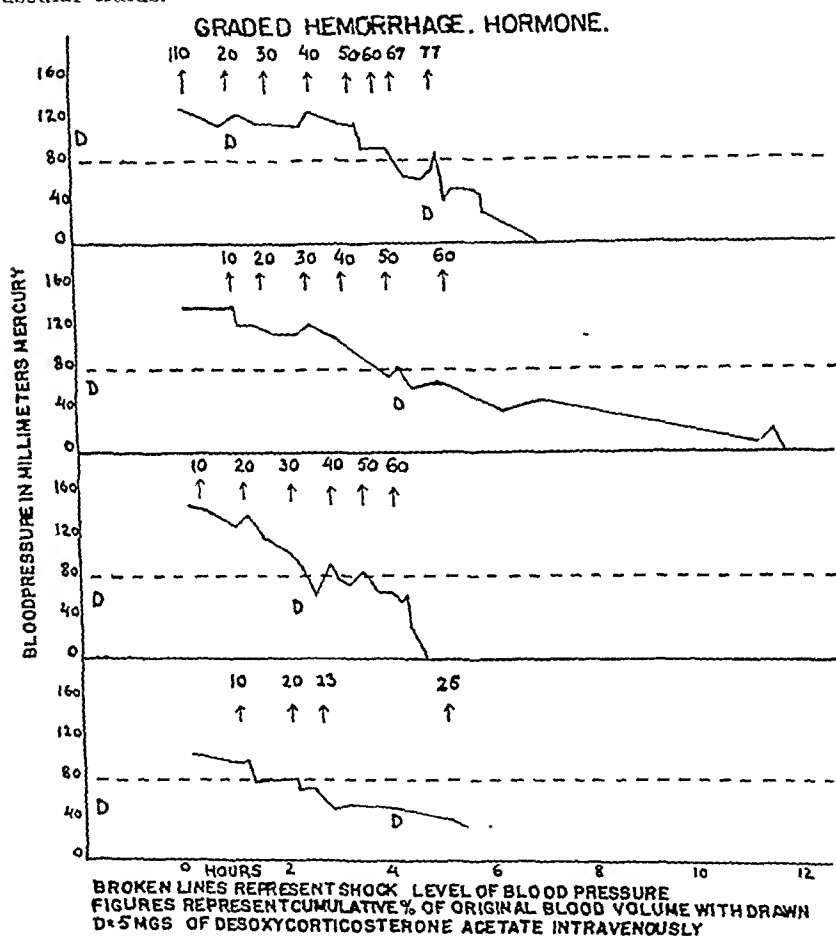


Fig. 3.

In preliminary experiments it was soon apparent that anesthetized dogs vary considerably in resistance to equal degrees of blood loss (Figs. 2 and 3) in so far as the development of shock is concerned. A shock level of blood pressure was reached within two to five hours and death occurred within eight hours in hormone-treated as well as in untreated animals. Nevertheless, in three out of four preliminary experiments with desoxycorticosterone acetate it was necessary to withdraw more blood to induce shock than in the control series (Fig. 3).

Plasma volume determinations were made as often as circumstances allowed on a subsequent series of twelve dogs during the period preceding the onset of shock. Three dogs received desoxycorticosterone

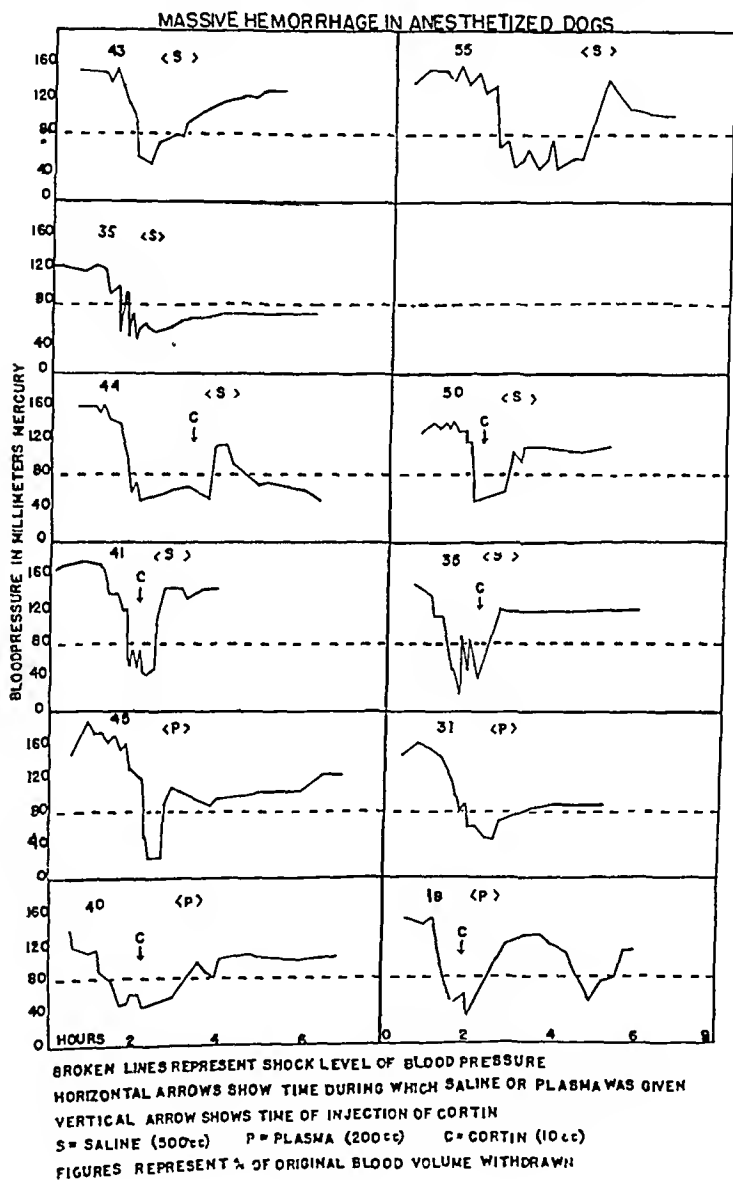


Fig. 4.

acetate and two others received cortin. The hormone was given intravenously two hours before the bleeding began. The remainder received no hormone. Even though it was not possible to obtain plasma volume determinations at corresponding intervals or after equal degrees of blood

loss, data of some value were secured. An inspection of Table IV shows that the hormone-treated dogs have no greater tolerance to graded hemorrhage than control animals, if they have as much. This is evident from (1) the amount of plasma removed in order to induce an irrecoverable shock level of blood pressure, (2) the fluid volume compensation for a given volume of plasma loss, (3) the net loss of plasma volume at the time of onset of the shock level of pressure, (4) the extent of the compensatory mobilization of plasma proteins, and (5) the absence in the hormone-treated dogs of a prolongation of the survival time.

The evidence is therefore against the usefulness of desoxycorticosterone acetate and of cortin in anesthetized animals subjected to massive or graded hemorrhage resulting in shock, *unless parenteral fluid is provided*. Given such a supply of fluid, cortin is advantageous while desoxycorticosterone acetate is not.

SUMMARY

1. Following a single massive hemorrhage (about 40 per cent of the total blood volume), anesthetized dogs go into shock. The survival time is not prolonged by cortin or desoxycorticosterone acetate.

2. When graded hemorrhage is carried out in anesthetized dogs, shock develops more slowly. The hormones do not facilitate the mobilization of extravascular fluids or proteins before the onset of shock, nor do they prolong the survival time.

3. Intravenous plasma and saline solution in such shocked animals are effective resuscitating agents. Cortin in addition to saline solution shortens the time required for restoration of the blood pressure to a sustained recovery level. To this extent cortin may be considered to have a slight usefulness in shock.

4. Normal unanesthetized dogs submitted to a single massive hemorrhage (some 40 per cent of the total blood volume) do not go into shock. The fluid-mobilizing capacity of such dogs during a four-hour period following the hemorrhage is not significantly increased by cortin or desoxycorticosterone acetate. Subcutaneous plasma alone or saline solution alone is equally effective. Cortin given with saline solution accomplished the greatest mobilization of all and therefore may be regarded as of some value in the therapy of acute plasma loss. Desoxycorticosterone acetate in these circumstances is ineffective.

5. The mobilization of protein into the circulating plasma after massive hemorrhage in unanesthetized dogs was not significantly improved by the hormones. However, following the injection of plasma into the subcutaneous tissues, the percentage recovery of lost circulating plasma protein was increased by cortin.

TABLE IV

THE EFFECT OF CORTIN AND DESOXYCORTICOSTERONE ACETATE ON THE RECOVERY OF LOST PLASMA VOLUME AND PLASMA PROTEINS DURING GRADED HEMORRHAGE IN ANESTHETIZED DOGS

EXPERIMENT NO.	DOSE OF HORMONE	ORIGINAL PLASMA		% RECOVERY OF % LOSS AT TIME OF SECOND PLASMA VOLUME DETERMINATION	ORIGINAL PLASMA VOLUME REMOVED AT ONSET OF SHOCK (%)	APPROX. NET LOSS OF PLASMA VOLUME AT ONSET OF SHOCK (IN %)	APPROX. NET LOSS OF PLASMA PROTEIN AT ONSET OF SHOCK (IN %)	SURVIVAL TIME IN HOURS	
		VOLUME REMOVED AT TIME OF SECOND* PLASMA VOLUME DETERMINATION (%)	PLASMA						
			VOLUME						PROTEIN
NO HORMONE									
1	-	42	16	(-7)	52	40	35	4½	
2	-	38	52	(-7)	48	30	20	5	
3	-	40	48	32	50	31	21	5¾	
4	-	35	42	14	46	26	15	4¾	
5	-	23	94	41	44	23	14	2¾	
6	-	21	19	(-14)	30	26	16	4	
7	-	20	13	0	40	37	17	¾	
DESOXYCORTICOSTERONE ACETATE									
8	9 mg.	26	(-30)	(-33)	29	43	34	6	
9	10 mg.	33	39	(-10)	33	26	20	5	
10	5 mg.	20	58	54	20	16	8	4	
CORTIN									
11	3 c.c.	22	50	47	22	30	11	3½	
12	4 c.c.	37	73	10	46	19	10	5¾	

*The first determination was made at the beginning of the experiment to obtain original plasma volume and plasma proteins.

*The first determination was made at the beginning of the experiment to obtain original plasma volume and plasma proteins.

CONCLUSION

Desoxycorticosterone acetate is not an effective agent in the therapy of shock due to hemorrhage. Cortin given alone is not an effective agent in the therapy of shock. If it is combined with parenteral fluids it exerts some beneficial influence in certain circumstances.

REFERENCES

1. Selye, H., Dosne, C., Bassett, L., and Whittaker, J.: On the Therapeutic Value of Adrenal Cortical Hormones in Traumatic Shock and Allied Conditions, *Canad. M. A. J.* 43: 1, 1940.
2. Ragan, C., Ferrebee, J. W., and Fish, G. W.: Effect of Desoxycorticosterone Acetate Upon Plasma Volume in Patients During Ether Anesthesia and Surgical Operation, *Proc. Soc. Exper. Biol. and Med.* 42: 712, 1939.
3. Weil, P., Rose, B., and Browne, J. S. L.: Reduction of Mortality From Experimental Traumatic Shock With Adrenal Cortical Substances, *Canad. M. A. J.* 43: 8, 1940.
4. Perla, D., Freiman, D. G., Sandberg, M., and Greenberg, S. S.: Prevention of Histamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortin) and Saline, *Proc. Soc. Exper. Biol. and Med.* 43: 397, 1940.
5. Gibson, J. G., and Evans, W. A., Jr.: Clinical Studies of the Blood Volume: I. Clinical Application of a Method Employing the Azo Dye "Evans Blue" and the Spectrophotometer, *J. Clin. Investigation* 14: 301, 1937.
6. Moore, Norman S., and Van Slyke, Donald D.: The Relationships Between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis, *J. Clin. Investigation* 8: 337, 1930.

THE THERAPY OF SHOCK IN EXPERIMENTAL ANIMALS WITH PLASMA PROTEIN SOLUTIONS*

I. CONCENTRATED PLASMA AS A HEMODILUTING AGENT IN SHOCK

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UNDER normal conditions the blood volume is principally composed of a fairly constant amount of red blood cells and plasma. In traumatic or posthemorrhagic shock there is a decrease in the effective circulating blood volume resulting from the partial loss of one or both of these constituents in varying amounts. Peripheral stagnation of blood in dilated vessels may further accentuate this abnormality.

It is becoming more apparent that generally the volume deficit per se is more important than the deficit of any one constituent, such as the red cells. This reasoning has resulted from the observation that a very copious hemorrhage is not fatal if the circulating volume be maintained with solutions not containing red blood cells. The anemia which results can usually be treated later without jeopardy to the patient when time is not such a valuable factor.

Although many mechanisms in shock are not well understood, the best therapeutic measure appears to be one which encourages the most rapid replacement of the circulating volume. The solutions most efficient in accomplishing this replacement contain plasma proteins, since such proteins tend to be retained within the vessels and, at the same time, are of a physiologic nature. The solutions that have been used¹⁻⁴ contain various protein concentrations, such as 15 to 20 Gm. per cent (concentrated), 5 to 7 Gm. per cent (normal), and 3 to 4 Gm. per cent (dilute).

The present communication demonstrates the ability of concentrated plasma to increase the blood volume in severe posthemorrhagic and traumatic shock in dogs. In these experiments (1940 to 1941) a few animals seemed to be harmed by plasma in normal and concentrated form. The apparent cause for these irregularities will be discussed below. Subsequent experiments (1942) dealing mainly with the apparent shifts of body fluid in shock and following therapy with concentrated and dilute serum are the subjects of a separate report.⁵

METHODS

Healthy dogs under nembutal anesthesia were used. The nembutal was given intravenously in doses of one grain for every five pounds of body weight. There were two groups. In the first group the animals

*Aided by a grant from Abbott Laboratories, North Chicago, Ill.
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were bled through a carotid artery cannula. Multiple bleedings over a period averaging three hours was the usual technique, although in a few instances one or two large bleedings were performed. The amount of blood removed ranged between 2.7 per cent and 5.4 per cent of the body weight with an average of 3.8 per cent. In the second group trauma to both lower extremities was the procedure used. Trauma was inflicted with a metal hammer as moderate blows. This procedure was repeated every fifteen to twenty minutes until the blood pressure reached shock levels. The first two trauma periods lasted five minutes and thereafter one- to three-minute periods were used. In this group two dogs were given histamine intravenously in addition to the trauma. In two other animals a tourniquet was applied about the extremities during trauma and later released. The average blood pressure during shock was 58 mm. Hg, ranging between 10 and 85 mm. The hemorrhagic group remained in shock for an average of 2.3 hours and the traumatic ones for an average of 1.5 hours before treatment.

The canine plasma used was obtained from citrated blood by conventional centrifugation in 250 c.c. bottles. During the collection of blood the donor dogs were subjected to intravenous nembutal anesthesia. All of the plasma was first desiccated from the frozen state by the adtevac process.⁶ The dry product was dissolved in one-fourth of the original volume and preserved in the frozen state. It was either administered as such or diluted back to normal with distilled water. Most often dog plasma was used but in isolated cases, as indicated in the tables, human plasma was given. The plasma, whether normal or concentrated, was injected rapidly into the femoral vein by means of a syringe, that is, 50 c.c. in one to five minutes' time.

The blood pressure was taken by means of a carotid cannula attached to a mercury manometer. The falling drop technique⁷ was used for the specific gravity determinations. The hemoglobin concentration was obtained by the Sanford-Sheard⁸ technique using a Leitz-Mass photoelectric colorimeter. The red cells were counted on each occasion in 20 hemocytometer squares. Wintrobe⁹ tubes were used in determining the hematocrits.

The blood samples were collected from either the jugular or the femoral vein. Heparin was used as an anticoagulant.

RESULTS

The essential part of the data is given in the tables. The results of the laboratory tests and the level of the mean arterial pressure are recorded in three periods. The first figures represent the control studies, those of the second group were taken during shock and just prior to treatment, and those of the third group were obtained an average of one and one-half hours after treatment, except in the animals that expired sooner, when the results immediately after treatment were recorded.

TABLE I
HEMORRHAGIC GROUP

NO. AND WEIGHT (KG.)	BLEEDING	TREATMENT	BLOOD SPECIFIC GRAVITY	PLASMA SPECIFIC GRAVITY	Hb. (GM. %)	R.B.C. (MILLIONS PER C.M.M.)	HEMATO-CRIT (%)	B.P. (MM. Hg)	REMARKS
I 10.0	300 c.c. One stage	95 c.c. 1/4 x conc. canine plasma	1.0329 1.0636 1.0554	1.0271 1.0281 1.030		6.58 8.24 6.77	40.4 54.1 34.0	140 45 120	Sacrificed 2 hr. later
II 6.2	250 c.c. Two-stage	90 c.c. 1/4 x conc. canine plasma	1.0508 1.0503 1.0430	1.0221 1.0261 1.0243		5.86 5.4 4.19	44.4 10 22.9	180 115	Sacrificed 11 hr. later
III 16.2	700 c.c. Multiple	150 c.c. 1/4 x conc. canine plasma		1.0318 1.0325		7.55 8.19	35.2 46.9 32.0	140 85 160 125	Sacrificed 19 hr. later
IV 9.0	364 c.c. Multiple	50 c.c. 1/4 x conc. canine plasma			14.45 12.0 9.5	6.53 5.34 3.9	41.6 36.4 28.0	150 70 110 85	Sacrificed 3.5 hr. later
V 8.0	377 c.c. Multiple	55 c.c. 1/4 x conc. canine plasma			12.25 11.4 7.2	5.74 4.31 3.24	37.6 31.1 22.5	135 50 105	Rapid downfall and death after last 30 c.c. Harmful effect
VI 7.5	261 c.c. Multiple	50 c.c. 1/4 x conc. human plasma; 100 c.c. saline solution by hypo.			12.0 9.3		34.0 21.5	160 40 exp.	Expired suddenly Harmful effect
VII 14.3	505 c.c. Multiple	90 c.c. 1/4 x conc. human plasma; 120 c.c. saline solution by hypo.		1.0246 1.0215 1.0239	15.85 12.95 9.8		44.0 36.1	155 70 135	Lived
VIII 8.0	305 c.c. Multiple	90 c.c. 1/4 x conc. human plasma			10.8 10.15 6.5		29.0 28.7 18.8	140 60 115	Sacrificed 3 hr. later
IX 6.5	250 c.c. Two-stage	360 c.c. Normal canine plasma	1.0511 1.0541 1.0476	1.0246 1.0228 1.0249		6.34 6.8 5.0	38.3 42.1 32.2	140 45 105	Lived
X 13.5	615 c.c. Multiple	600 c.c. Normal canine plasma	1.0577 1.0450			8.94 7.5 4.8	39.2 28.4 18.6	190 85 125	Expired approximately 8 hr. later

There were 20 animals in the posthemorrhagic shock group, 16 of which received concentrated plasma and 4, normal plasma. In the traumatic group 6 dogs received concentrated plasma and 3, normal plasma. The volumes of normal and concentrated plasma given were calculated so as to have comparable amounts of protein. In the tables the essential data from 10 animals in the hemorrhagic group and 6 in the traumatic group are given. The data in the other 13 animals were similar to those presented in the tables.

The animals were all in deep shock as demonstrated by the depression in the blood pressure, the collapsed peripheral veins, and the thready and very weak femoral artery pulse. Survival time was not determined and the observations were confined to the interval a few hours after treatment.

Seven of the animals in posthemorrhagic shock showed slight hemoconcentration. The others displayed slight hemodilution. In the traumatic shock group hemoconcentration failed to occur in only one animal.

It was observed that concentrated plasma caused hemodilution in each case as reflected by a drop in the whole blood specific gravity, a decrease in the red cell count, hemoglobin concentration, and hematocrit. This hemodilution was observed to occur in several instances within five minutes after the injection. During the hemodilution the plasma specific gravity remained about the same, meaning that fluid was withdrawn into the circulation. The elevation in the blood pressure paralleled this hemodilution. It was also observed that the injection of normal plasma with a comparable amount of protein content produced similar results.

As is pointed out in the table, several of the animals responded unfavorably to concentrated plasma. These ill effects were represented by a rigor, lack of elevation of the blood pressure, or even sudden death. These irregular findings could not be understood at first because during the same period very favorable results were being obtained from the use of concentrated plasma in clinical shock.^{4, 10}

In subsequent experiments on normal unanesthetized animals¹¹ definite ill effects were encountered when concentrated plasma was injected rapidly intravenously. There was usually transient but very severe tetany. Most animals subsequently became ataxic, exhibited carpopedal spasm, vomited or retched severely, became lethargic, and occasionally fell asleep. These ill effects would last a varying period of time, and then the animal appeared quite normal. By considering the amount of sodium citrate used as anticoagulant it became apparent that the concentrated plasma contained at least 2 per cent sodium citrate. When such quantities of sodium citrate were given to normal animals similar tetany was observed. As a further check on the citrate effect, it was

TABLE II
TRAUMATIC GROUP

NO. AND WEIGHT (Kg.)	METHOD	TREATMENT	BLOOD SPECIFIC GRAVITY	PLASMA SPECIFIC GRAVITY	HB. (GM. %)	R.B.C. (MILLIONS)	HEMATOCRIT (%)	B.P. (MM. HG)	REMARKS
I 8.8	Trauma	100 c.c. 4 x conc. canine plasma	1.0493 1.0646 1.0516	1.0219 1.0367 1.0312		5.46 4.6	32.3 20.0	145 50 120 50	Expired 1.5 hr. after treatment
II 7.0	Trauma	90 c.c. 4 x conc. canine plasma	1.0531 1.0599 1.0455	1.0282 1.0322 1.0281		5.96 6.25 3.46	36.2 17.5	155 80 165	Suddenly expired after B.P. to 165 Harmful effect
III 16.4	Trauma and tourniquet	100 c.c. 4 x conc. canine plasma			14.4 9.95 4.65	3.97 3.55 2.56	22.0 22.0 19.0	130 55 110	Expired 3 hr. later
IV 9.9	Trauma and histamine, 13 c.c. 0.1% solution I.V.	100 c.c. 4 x conc. canine plasma	1.0527 1.0543	1.0280 1.0237		6.64 6.26	29.4 38.2	150 50 120	Expired Harmful effect
V 10.8	Trauma	180 c.c. Normal canine plasma	1.0557 1.0671 1.0442	1.0228 1.0325 1.0232		6.7 7.7 4.5	38.4 32.6 24.0	160 70 110	Sacrificed 2.5 hr. later
VI 9.4	Trauma and histamine, 12.5 c.c. 0.1% solution I.V.	400 c.c. Normal canine plasma	1.0529 1.0548 1.0456	1.0266 1.0237 1.0224				160 85 120	Sacrificed one hr. later

demonstrated that the administration of neutralizing amounts of calcium chloride with, or shortly before, the concentrated plasma prevented the tetany. Likewise, the administration of concentrated serum without citrate failed to produce tetany. However, the ataxia, retching, vomiting, and lethargic appearance persisted. Since the blood had been collected from donor dogs under nembutal anesthesia, it was assumed that a small quantity of nembutal was being given in the plasma. This assumption was shown to be correct by the production of similar ill effects when small doses of free nembutal were administered intravenously to normal animals. As a final check to these two types of reactions the dog plasma containing citrate-nembutal was dialyzed at low temperature against normal saline solution. After sufficient dialysis the plasma did not produce these ill effects.

TABLE III

Illustrating the effect of citrated dog plasma (at least 2% sodium citrate) containing nembutal when administered intravenously in concentrated form (4 × conc.) to a normal dog under nembutal anesthesia (4 gr. nembutal intravenously).

TIME (P.M.)	AMOUNT INJECTED CONC. CANINE PLASMA	B.P. (MM. HG)	REMARKS
2:47		160	Weight 7.8 kg. Dog under nembutal anesthesia
3:06	10 c.c.	90-140	Wide fluctuations of Hg manometer
3:07	10 c.c.	120-140	Severe tetany began, deep breath, marked rigidity
3:08 to 3:12	55 c.c.	60-165	Tetany persists
3:14		30	Respirations almost ceased, shock-like state
3:32		135	Normal respirations
5:50		140	Appears normal, complete recovery
Total	75 c.c.		

It was then evident that the occasional ill effects in the shock group were due to two causes: First, the rapid administration of a relatively large amount of sodium citrate, which before its oxidation bound sufficient calcium to produce tetany. It is known that such rapid calcium ion deficiency may produce cardiac embarrassment by vagal inhibition or vagal paralysis.^{12, 13} Second, the barbiturate effect could be an aggravating factor in animals in deep shock, although not at all dangerous to normal animals. It has been observed that following a favorable blood pressure response in experimental shock therapy the animal may begin to awaken from the comatose state. If at this time a small amount of nembutal is given intravenously there may be a definite drop in the blood pressure. When the animal is in shock these ill effects may be unnoticed and the plasma protein solution may be considered to be ineffective therapeutically. Variations in animal tolerance, variations in the plasma, and the masking effect of the depressed condition of animals in shock may account for the fact that all experiments did not

demonstrate these ill effects. These 50 to 100 c.e. doses in 10 kg. dogs would be comparable to 500 to 1,000 c.e. doses in an 80 kg. person. It is very difficult to administer such huge doses of concentrated plasma to a human being in such a short period of time. Therefore, similar complications in adult human beings would not be expected from the administration of concentrated plasma. However, in children we⁴ have observed such calcium binding effect with transient tetany.

DISCUSSION

These studies illustrate the ability of concentrated plasma to produce hemodilution in animals in deep hemorrhagic and traumatic shock. The hemodilution considerably exceeds that which would be expected from the injection of the decreased volume of the concentrated plasma alone. Therefore, there must be an increase in the blood volume resulting from a withdrawal of fluids into the circulation at the capillary beds. This indicates either that the fluid shift occurs through damaged capillaries or that undamaged capillaries are available in deep shock, through which interstitial fluid may be drained into the vascular system.

In shock the therapeutic efficiency of any plasma protein solution depends largely on its protein content, since it is the protein molecule that maintains the plasma volume. Hence, an equal degree of hemodilution is obtained when normal or concentrated plasma of comparable protein content is given to different animals at similar rates of injection. These observations were first mentioned by Magladery, Solandt, and Best.¹⁴ However, the action of these two agents is different, for, whereas concentrated plasma or serum causes an internal shift of fluids, a normal plasma injection merely adds more fluids. Recent evidence suggests that cells take up water in experimental hemorrhagic¹⁵ and freezing shock.⁵ The possibility that concentrated plasma may reclaim such water¹¹ appears very logical. It seems that the withdrawal of misplaced fluids by the use of concentrated plasma is more of a reversal of certain shock mechanisms than would be expected from the external addition of normal plasma.

It may be stated then that the efficacy of any protein solution in the treatment of shock depends upon the total protein content; the protein concentration, which determines its ability or lack of ability to shift fluids from an extravascular to an intravascular position; and its rate of administration.

It has recently been stated¹⁶ that large volumes of dilute plasma are more beneficial in the treatment of shock than normal or concentrated plasma, and a failure of response was observed in certain animals given concentrated plasma. This question is discussed in other publications.^{5, 17} Suffice it to mention at present that plasma protein solutions varying in protein concentration should be compared not only ac-

according to comparable volumes and comparable protein content, but also according to rate of injection. Whether the plasma contains sodium citrate or barbiturate should be mentioned. Obviously, if a deleterious substance is present in the plasma, its injection may be innocuous in dilute form due to the slowness of administration, and quite harmful in concentrated form because a greater quantity of the substance is ordinarily given per unit of time.

The term "four times concentrated plasma" signifies that the dry product was dissolved in one-fourth of the original volume. The protein content of such a concentrate depends on the protein concentration of the original citrated plasma prior to desiccation. In spite of the resulting variation in the protein content of the original citrated plasma, the final concentrated product is usually loosely compared with the osmotic property of normal plasma taken to contain 7 Gm. per cent of proteins. Such terminology has given rise to much confusion. It seems essential to drop the term "four times concentrated plasma" and speak directly of its protein content in grams per cent. Unfortunately, in the present studies we failed to take these considerations into account. As a result of this, certain disparities appear in the data of this report. For instance, when the original blood volume is calculated on the basis of body weight and subsequent volume changes are calculated according to changes in the hemoglobin concentration or hematocrit, it is revealed that the volume increases following the concentrated plasma injections are smaller than would be expected from the injection of true four times concentrated plasma (approximately 25 Gm. per cent). Obviously the concentrated plasma solutions used in the present studies contained smaller amounts of protein than might be expected from the use of the term four times concentrated plasma, which is used to define a solution obtained by dissolving the solid residue in one-fourth of the original volume. Assuming that all of the plasma given remained within the blood stream after the equilibration of its protein content, an analysis of the data from two experiments might clarify these points. Following is an example:

Dog No. VIII

Weight	8	kg.
Calculated blood volume (9% body weight)	720	c.e.
Control hematocrit	29.0	%
Control red cell volume	208.8	c.e.
Volume red cells bled	88.5	c.e.
Shock red cell volume	120.3	c.e.
Shock blood volume ($120.3 \div 28.7$)	419	c.e.
After treatment blood volume ($120.3 \div 18.8$)	640	c.e.
Increase in plasma volume	221	c.e.
Expected increase 90×4	360	c.e.

On the same basis dog No. III showed a calculated volume increase of 267 c.e. out of an expected increase of 600 c.e. Such calculations are influenced by other factors, and therefore are not strictly accurate but

can be used to demonstrate the relative trend in the experiments and show that the volume increase was much greater than would be expected from the volume of concentrated plasma alone. This method of calculating volume changes cannot be used in the traumatic shock group because the volume of red cells lost is a totally unknown quantity.

In a subsequent report⁵ it is shown that in the treatment of experimental shock with concentrated serum the plasma volume increase is directly proportional and equivalent to the grams of protein injected.

Most workers in this field are willing to agree that concentrated plasma given in standard glass syringes can be handled more rapidly and with greater ease than other more bulky plasma solutions, such as normal or dilute plasma. However, its therapeutic efficiency is questioned, the dangers of reactions are emphasized, and it is stated that dehydration may be a harmful sequel. Therapeutically concentrated plasma is capable of producing hemodilution in direct proportion to its protein content. A plasma that is free from agglutinins, bacteria, and pyrogens and that has been prepared by desiccation from the frozen state, in our experience¹⁰ will not produce reactions when given in concentrated form. Dehydration following the injection of concentrated solutions depends on the type of solution given. For instance, when concentrated glucose is given intravenously it draws fluids from the tissues and thus increases the plasma and blood volume. At the same time because the plasma is diluted its composition is altered. The kidneys, being more concerned with plasma composition¹⁸ rather than volume, reject the added water in the urine. The glucose is either taken up by the liver or metabolized. Therefore, water is lost from the body, the glucose is removed from the blood stream, and dehydration may eventually result.¹⁹ When concentrated plasma is injected it draws fluids from the tissues but the plasma composition remains about normal. The kidney will not reject the added fluid readily and the mechanisms of dehydration are thus avoided. In nephrosis or low protein edema the diuresis seems to be related to a decrease in sodium intake plus a greater renal plasma flow that is associated with plasma therapy.

Concentrated plasma should receive more consideration in the treatment of shock. It has a definite physiologic basis for its rationale. The ease of handling gives it tremendous military advantages.

CONCLUSIONS

1. Concentrated plasma produces hemodilution rapidly in severe posthemorrhagic and traumatic shock in dogs.

2. The hemodilution is due to the shift of fluids from an extravascular to an intravascular location as shown by the lack of change in plasma specific gravity.

3. Normal plasma with comparable protein content is capable of producing hemodilution.

4. The difference in the action of concentrated and normal plasma is pointed out.

5. Two distinct causes for untoward reactions in experimental animals after the injection of concentrated plasma are discussed.

6. The importance of concentrated plasma in military practice is re-emphasized and certain objections by other workers are briefly discussed.

REFERENCES

1. Elliot, J., Busby, G. F., and Tatum, W. L.: Some Factors and Observations on the Preparation and Preservation of Dilute Plasma, *J. A. M. A.* 115: 1006, 1940.
2. Strumia, M. M., Wagner, J. A., and Monaghan, J. F.: The Use of Citrate Plasma in the Treatment of Secondary Shock, *J. A. M. A.* 114: 1337, 1940.
3. Levinson, S. O., Rubovits, F. E., and Necheles, H.: Human Serum Transfusions, *J. A. M. A.* 115: 1163, 1940.
4. Hill, J. M., Muirhead, E. E., Ashworth, C. T., and Tigertt, W. D.: The Use of Desiccated Plasma With Particular Reference to Shock, *J. A. M. A.* 116: 395, 1941.
5. Muirhead, E. E., Ashworth, C. T., Kregel, L. A., and Hill, J. M.: Shock Therapy: Fluid Distribution in Body and Its Relation to Treatment With Concentrated and Dilute Serum and Saline Solutions. Unpublished.
6. Hill, J. M., and Pfeiffer, D. C.: A New and Economical Desiccating Process Particularly Suitable for the Preparation of Concentrated Plasma and Serum for Intravenous Use: The Adtevac Process, *Ann. Int. Med.* 14: 201, 1940.
7. Barbour, H. G., and Hamilton, W. F.: Falling Drop Method for Determining Specific Gravity, *J. Biol. Chem.* 69: 625, 1926.
8. Sanford, A. H., and Sheard, C.: The Determination of Hemoglobin With the Photoelectrometer, *J. Lab. & Clin. Med.* 15: 483, 1929.
9. Wintrobe, M. M.: Simple and Accurate Hematocrit, *J. Lab. & Clin. Med.* 15: 287, 1929.
10. Muirhead, E. E., and Hill, J. M.: The Advantages and Clinical Use of Desiccated Plasma Prepared by the Adtevac Process, *Ann. Int. Med.* 16: 286, 1942.
11. Ashworth, C. T., Muirhead, E. E., and Hill, J. M.: The Effect of Hypertonic Plasma on the Body Fluids of Normal Experimental Animals, *Am. J. Physiol.* 136: 194, 1942.
12. Shafer, G. D.: Temporary Paralysis of the Vagus Mechanism in the Turtle by Sodium Citrate and Sodium Oxalate, *J. Pharmacol. & Exper. Therap.* 58: 264, 1936.
13. Shafer, G. D., and Crimson, J. M.: Paralyzing Effects of Sodium Citrate on the Cardiac Vagus and on Heart Muscles of the Cat, *J. Pharmacol. & Exper. Therap.* 58: 274, 1936.
14. Magladery, J. W., Solandt, D. Y., and Best, C. H.: Serum and Plasma in the Treatment of Hemorrhage in Experimental Animals, *Brit. M. J.* 2: 249, 1940.
15. Ashworth, C. T., and Kregel, L. A.: Changes in the Body Water and Electrolytes in Shock, *Arch. Surg.* In press.
16. Mahoney, E. B., Kingsley, H. D., and Howland, J. W.: The Treatment of Experimental Shock by the Intravenous Injection of Dilute, Normal and Concentrated Plasma, *Surg., Gynec. & Obst.* 74: 319, 1942.
17. Muirhead, E. E., Hill, J. M., and Ashworth, C. T.: The Use of Human Plasma Protein Solutions in Surgery. Unpublished.
18. Smith, H. W.: *The Physiology of the Kidney*, New York, 1937, Oxford University Press, p. 150.
19. Keith, N. M.: Experimental Dehydration, *Am. J. Physiol.* 68: 80, 1924.

A MODIFIED TECHNIQUE OF SURGICAL LIGATION OF PATENT DUCTUS ARTERIOSUS

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IN 1939, Gross and Hubbard² reported the first successful ligation of a patent ductus arteriosus. Stimulated by this brilliant surgical achievement, the operation soon was attempted by others with the result that the effectiveness of ductal ligation in correcting circulatory abnormality quickly became established. The technique described by Gross¹ has been generally employed up to the present time, and apparently has proved quite satisfactory. The chief dangers which attend operation are (1) hemorrhage as the result of inadvertent injury of the ductus or pulmonary artery, and (2) injury of the left recurrent laryngeal nerve. Hemorrhage is most apt to occur as the posteromesial wall of the ductus is being separated from the adjacent, main trunk and right branch of the pulmonary artery. (This portion of the ductal wall faces away from the operator, and therefore cannot be visualized completely.) Thus, its separation from the pulmonary artery constitutes a relatively "blind" procedure, during which either of the aforementioned structures may be inadvertently torn. In an attempt to avoid such accidents, ductal dissection of necessity must be performed carefully and unhurriedly. (Gross has reported a case in which almost two hours were spent in performing this step of the procedure, alone.) Gross has stressed the necessity for careful and complete exposure of the left recurrent laryngeal nerve, as a guide to the location of the ductus. If injury to the nerve is to be avoided, considerable time may have to be expended in this dissection also. The operation for ligation of patent ductus arteriosus therefore is one which, in general, is apt to be time consuming if serious complications are to be avoided.

In 1940, Vesell and I³ reported the first case of subacute bacterial endarteritis complicating patent ductus arteriosus, in which recovery followed surgical treatment. During the same year we reported our experiences in the surgical treatment of three additional cases,⁴ and emphasized that in the presence of infection the likelihood of accidental hemorrhage is increased considerably. The latter is attributable to two important pathologic features which may accompany the superimposed infection: (a) friability of the ductus, as the result of atheromatous and infectious disease changes; and (b) periarteritis, which renders the ductus very firmly adherent to the surrounding structures, the most important of which is the pulmonary artery. Furthermore, since our four

patients were adults, and the duration of the congenital lesion therefore longer, the pulmonary artery was relatively more dilated, thin walled, and susceptible to accidental injury than in the case of children. Thus in spite of the fact that great care was exercised in dissecting out and manipulating the ductus, hemorrhage occurred in three instances. Of these, two patients succumbed upon the operating table. In the third, profuse bleeding from a tear in the ductus was successfully controlled. (The last patient recovered and has been entirely free of all evidence of subacute bacterial endarteritis since operation, almost two years ago.)

With the realization that we were dealing with a disease which still is considered to be almost invariably fatal under conservative forms of therapy, I was encouraged to continue my surgical efforts, despite the fact that operation had proved to be so hazardous. It was my hope that the latter might be rendered more safe by modifying the operative technique; and accordingly, when the next patient with patent ductus arteriosus complicated by subacute bacterial endarteritis was presented for surgical treatment, a somewhat different type of procedure was carried out. Shortly thereafter another infected case was operated upon, with the same technique. Both of these patients apparently have been cured of the bacterial infection;^{5, 6} in neither case was the surgical procedure attended by hemorrhage and the time consumed in operating was reduced materially. (In the latter case, operation was performed in fifty-five minutes). Since the avoidance of hemorrhage and the shortening of operation appear to be attributable chiefly to the modified technique, the latter seems worthy of description. It is applicable not only to infected cases but also to uninfected cases, and is based upon a number of principles which themselves are dictated by certain anatomic and pathologic findings. The latter are as follows: (a) the aorta is by far the strongest structure and the one most resistant to injury in the immediate operative field; (b) the aortic end of the ductus is normally the strongest portion of the ductus and the portion which is least apt to be affected by atheromatous and infectious changes; and (c) it is easier and safer to free a vessel which is firmly adherent to some surrounding structure by carrying out the procedure in a plane of cleavage within the adventitia, than by attempting to strip the intact vessel from the surrounding tissues.

In sequential order, the steps of the modified operation consist of: (a) Entering an inter- or subadventitial plane of dissection, upon the aorta, close to the aortic end of the ductus; (b) "tunnelling," within the above plane (upon the aorta), completely behind the aortic end of the ductus; (c) developing the plane from the aorta, to the posteromesial wall of the ductus itself.

The procedure is performed under rather complete visualization, and by keeping within the adventitial plane of the aorta and adjoining ductus, injury to the pulmonary artery and recurrent laryngeal nerve is minimized.

The operative entry of the thorax and the exposure of the aortic arch and pulmonary artery are performed in the manner described by Gross. (Although Gross has recommended entry of the thorax routinely through the second intercostal space, in certain cases the lower border of the aortic arch is seen in the x-ray film to lie at or near the level of the third interspace. Under such circumstances, an incision in the third interspace affords a more direct approach to the ductus.) The upper end of the trunk of the dilated pulmonary artery is identified and dissected from the aortic arch. After this has been accomplished, the position of the ductus is determined by palpating for the point of maximal thrill in the region of the concavity of the aortic arch. The pulmonary artery, which in adults often completely obscures the aortic arch from view (Fig. 2),

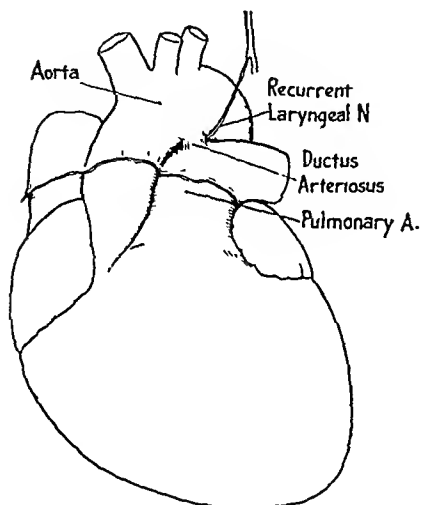


Fig. 1.

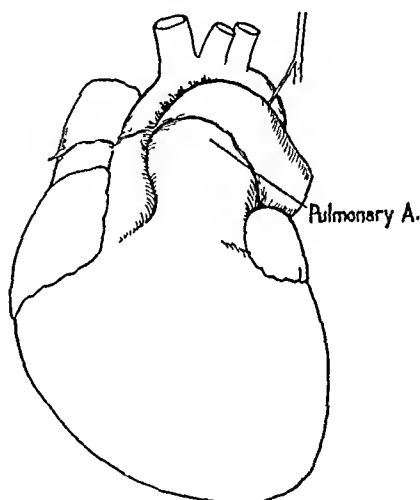


Fig. 2.

Fig. 1.—Schematic drawing to illustrate relative size of the aorta, pulmonary artery, and ductus arteriosus, shortly before birth.

Fig. 2.—Schematic drawing to illustrate the findings in cases of patent ductus arteriosus of long duration (as in adults). Note the marked dilatation of the pulmonary artery. (The latter often obscures the aorta completely.) The ductus arteriosus is not visible.

then is gently displaced downward as far as possible and held in this position by a ribbon retractor (Fig. 3). This exposes the general region of the ductus. The anterolateral surface of the ductus next is exposed by removing the overlying areolar tissue and lymph nodes. The angle between the upper surface of the ductus and the aorta, and the angle between the lower surface of the ductus and the aorta then are exposed carefully in the same manner. Care is taken to avoid the proximal portion of the recurrent laryngeal nerve as it leaves the trunk of the vagus near the lower of the two angles mentioned above. The adventitia of the aorta at the upper angle (Fig. 4, A) is grasped with a toothed forceps close to the ductus, and incised with fine scissors. A fine, curved, cystic duct clamp then is passed into the incision in the aortic adventitia

and advanced slowly and progressively, downward and laterally, along the posterior wall of the aorta immediately adjacent to the aortic end of the ductus. As this plane is developed, a narrow ribbon retractor is in-

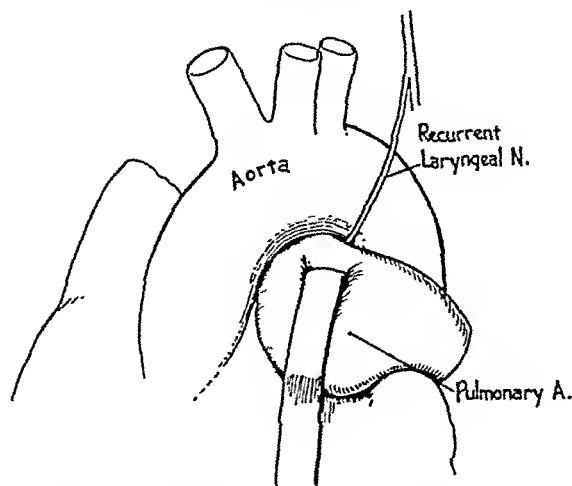


Fig. 3.—First stage of the author's modified operative procedure. The pulmonary artery has been dissected from the aorta and is displaced downward by a retractor. After removing areolar tissue and lymph nodes from the region of the concavity of the aortic arch, the ductus arteriosus comes into view.

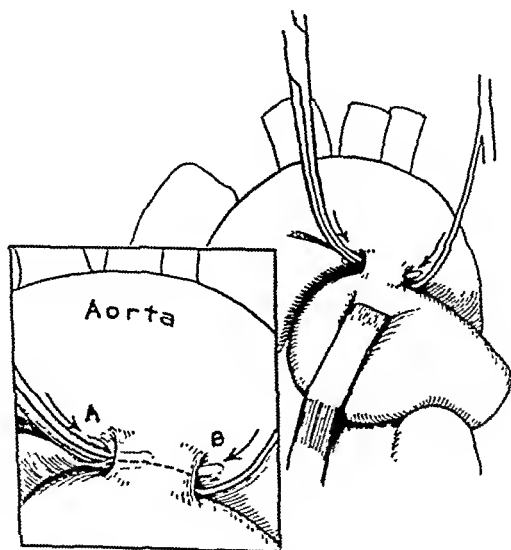


Fig. 4.—Operation continued. An incision is made in the aortic adventitia at A. A fine curved cystic duct clamp is introduced into the adventitial incision and gradually passed downward and laterally (upon the aorta) as far as possible. A similar dissection is begun at B and carried upward until a "tunnel" has been completed (beneath the adventitia of the aorta) behind the aortic end of the ductus.

roduced; and the aortic adventitial tissue, which has been stripped free, is retracted medially. The origin of the right branch of the pulmonary artery, which lies outside (mesial to) the freed adventitia thus

is retracted automatically (Fig. 5). Once the plane of cleavage has been entered properly, tiny gauze sponges held in small curved hemostats are employed as atraumatic dissectors. As the dissection progresses along the posterior wall of the aorta, it also is extended for a short distance behind the ductus. The retractor which holds the stripped adventitial tissue and pulmonary artery aside is advanced progressively deeper as the posteromesial surface of the aortic end of the ductus is freed. As a result, the stripping of this portion of the ductus is accomplished under fairly complete visualization. After the separation of the aortic end of the ductus has been carried from above downward as far as room will permit, attention is directed to the angle between the lower surface of the ductus and the aorta. The aortic adventitia in this area (Fig. 4, *B*) is incised near the ductus. As the assistant holds the edges of the adventitial incision apart, the curved,

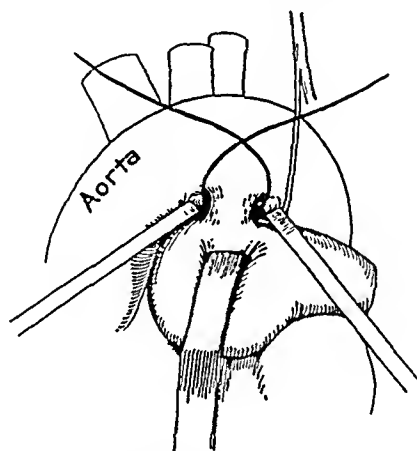


Fig. 5.—After the "tunnel" within the adventitia of the aorta has been completed, the plane of dissection is carried onto the posteromesial surface of the ductus. Note that the retractors within the adventitia hold aside the right branch of the pulmonary artery and the recurrent laryngeal nerve without actually coming into contact with either of those structures. The ligature has been passed behind the ductus.

cystic duct clamp previously mentioned is introduced into the proper plane and passed gently upward behind the aorta adjacent to the ductus. The dissection then is extended onto the aortic end of the ductus, in the manner already described. As the adventitia, which has been separated from the aorta and the aortic end of the ductus, is retracted, the recurrent laryngeal nerve which lies immediately below and outside it is automatically held aside without coming into actual contact with the dissecting instrument (Fig. 5). A small ribbon retractor once more is introduced into the upper adventitial incision as deeply as possible from above downward, and by retracting the freed adventitia and subjacent pulmonary artery mesially, the posteromesial surface of the ductus again is exposed. The tip of the curved clamp which is being directed from below upward, behind the

ductus, now can be readily visualized and the freeing of the postero-mesial ductal wall completed. In ligating the ductus (Fig. 6), two heavy silk ligatures are employed. One of these is placed directly adjacent to the aorta and the second nearby. In view of the minimal infectious changes and the greater thickness of the ductal walls in this area, accidental tearing of the ductus during ligation, and cutting through of the ductal ligatures, subsequently, is minimized. Furthermore, a ligation of the ductus very close to the aorta has the additional advantage of excluding infected vegetations within the interior from direct contact with the aortic blood current. (The role of surgical ligation in the cure of infected patent ductus will not be set forth here, but will be discussed in detail in a forthcoming paper which will deal with the rationale of surgical treatment.)

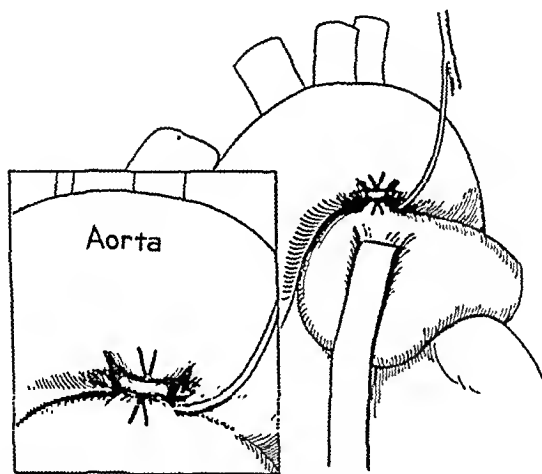


Fig. 6.—Final stage of procedure. Double ligatures tied about the ductus, as close to aortic end as possible.

Following ligation of the ductus, the local site is sprinkled with 1 to 2 Gm. of powdered sulfathiazole or sulfapyridine. The mediastinal pleura is left open, in order to permit fluid exudate to drain freely into the pleural cavity. The thoracic cage and parietes are closed in layers, the lung being inflated by the anesthetist just as the closure of the pleural cavity is completed.

SUMMARY AND CONCLUSIONS

1. The chief dangers attending operation upon patent ductus arteriosus are (a) hemorrhage as the result of inadvertent injury of the ductus or pulmonary artery, and (b) injury of the left recurrent laryngeal nerve.
2. In the presence of subacute bacterial endarteritis, the likelihood of accidental hemorrhage may be greatly increased as the result of friability

of the ductus and its firm adherence to the surrounding structures, especially the trunk and right branch of the pulmonary artery.

3. In order to minimize the likelihood of injuring the ductus, pulmonary artery and recurrent laryngeal nerve, the original operative technique described by Gross, has been modified.

4. These modifications consist of: (a) entering an inter- or subadventitial plane of dissection, upon the aorta, close to the aortic end of the ductus; (b) "tunnelling," within the above plane (upon the aorta), completely behind the aortic end of the ductus; (c) developing the plane from the aorta to the posteromesial wall of the ductus itself.

5. Of four operative cases of patent ductus arteriosus complicated by subacute bacterial endarteritis reported originally, serious hemorrhage occurred in three. In two recent similar cases operated upon with the technique herein described, hemorrhage did not occur and the time required for operation was reduced materially.*

6. The improved technique is applicable both to infected and uninfected cases of patent ductus arteriosus and should reduce the hazards of operation considerably.

REFERENCES

1. Gross, R. E.: A Surgical Approach for Ligation of a Patent Ductus Arteriosus, *New England J. Med.* 222: 510, 1939.
2. Gross, R. E., and Hubbard, J. P.: Surgical Ligation of a Patent Ductus Arteriosus, *J. A. M. A.* 112: 729, 1939.
3. Touroff, A. S. W., and Vesell, H.: Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus. Recovery Following Surgical Treatment, *J. A. M. A.* 115: 1270, 1940.
4. Touroff, A. S. W., and Vesell, H.: Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus, *J. Thoracic Surg.* 10: 59, 1940.
5. Touroff, A. S. W., Vesell, H., and Chasnoff, J.: Operative Cure of Subacute Streptococcus Viridans Endarteritis Superimposed on Patent Ductus Arteriosus. Report of the Second Successful Case, *J. A. M. A.* 118: 890, 1942.
6. Touroff, A. S. W., and Tuchman, L. R.: Subacute Streptococcus Viridans Endarteritis Superimposed on Patent Ductus Arteriosus. Spontaneous Recovery. Recurrence After 12 Years. Recovery Following Surgical Treatment, *Am. Heart. J.* 23: 857, 1942.

*Since submitting this paper for publication, two more cases of infected patent ductus arteriosus have been operated upon successfully.

LIGATION OF A PATENT DUCTUS ARTERIOSUS: REPORT OF A SUCCESSFUL CASE

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THE ductus arteriosus in fetal life serves the important function of shunting blood from the pulmonie artery to the aorta, thus bypassing the lungs. Incomplete expansion of the lungs produces a high resistance in the pulmonary vascular bed. When the child is born and the lungs expand, the peripheral pulmonary resistance to blood flow is lowered. Pressure in the aorta then is higher than pressure in the pulmonary artery. The ductus normally closes and all the blood in the pulmonary artery passes through the lungs to be aerated. If the ductus arteriosus fails to close, a reversal of flow takes place, and blood passes from the aorta to the pulmonary artery through the ductus. The patient then possesses what is essentially an arteriovenous aneurysm.

Patten¹ claims the degenerative intimal changes take place in the ductus arteriosus during the latter part of fetal life, and it is his belief that increasing amounts of blood flow through the lungs even before birth.

Christie² studied a large series of routine autopsy specimens from infants to determine when the ductus arteriosus is normally obliterated. In infants of one month, an open ductus was found in 44 per cent; at two months it was open in 12 per cent; and at eight months it was open in 2 per cent. In a small percentage of cases, the ductus remained open permanently.

Barelay^{3, 4} and his co-workers performed detailed x-ray studies on lambs delivered by Cesarean section, as well as on adult animals. They concluded that the ductus closes functionally within five minutes after delivery. The x-ray technique of visualizing the ductus arteriosus does not seem applicable to clinical use at present.

Gross⁵ sets an arbitrary time limit of one year, believing that an open ductus after that time should be regarded as abnormal. He also considers the etiology of a patent ductus arteriosus and discusses three interesting possibilities. The position and direction of the vessel is important. Usually it enters the aorta at an acute angle. As the acuteness of the angle decreases, the ductus is more and more exposed to intra-aortic pressure. If the angle becomes a right or even an obtuse angle, the force of intra-aortic pressure can readily be exerted to maintain patency of the lumen of the ductus. In his operative experience, Gross

has repeatedly observed this deviation from the usual acute angle. The second possibility is a defect in the elastic fiber of the media, decreasing the contractibility of the ductus. A third possibility is a deficient neurovascular tonus. Gross points out that the discussion of these possibilities does not apply to cases in which another congenital defect acts to maintain an open ductus arteriosus as a compensatory mechanism.

PATHOLOGIC PHYSIOLOGY

Hazards of a Patent Ductus Arteriosus.—The patent ductus arteriosus may be accompanied by other congenital abnormalities. Such pathologic combinations come within the scope of this presentation only as considerations in the differential diagnosis of patent ductus arteriosus. A patent ductus arteriosus can and does exist as a single congenital cardiac anomaly. The hazards of its presence alone are sufficient to justify operation in selected cases.

Eppinger and Burwell,⁶ with Gross,⁷ studied the effects of the patent ductus on the heart and circulation in six patients before and after ligation of the ductus. They pointed out that in the presence of a patent ductus arteriosus, the flow is from the aorta to the pulmonary artery. No flow from the pulmonary artery to the aorta takes place, and hence the patient is not cyanotic. From blood samples taken from the vessels both before and after ligation, they estimated that the volume of blood flowing from the aorta to the pulmonary artery varied from four to nineteen liters per minute. In other words, the shunt diverted from 45 to 75 per cent of all blood pumped into the aorta by the left ventricle. They also found that the left ventricle expelled from two to four times the volume of blood expelled by the right ventricle over a given period of time. Obviously the adjustment of the circulation to the patent ductus arteriosus is made by an increase in left ventricular output. If compensation is incomplete, there may be a diminution of blood flow to the periphery. These studies clearly show the tremendous strain a patent ductus imposes upon the heart.

The hazards of a patent ductus arteriosus are well demonstrated by studies of the life expectancy of such patients. Maude Abbott⁸ cites ninety-two patients in whom the mean age of death was twenty-four years. Since the series includes twenty patients who died in infancy, the mean age of death is somewhat confusing.

Jones, Dolley, and Bullock⁹ reviewed seventy-six cases from the literature and added four from personal experience, a total of eighty cases. All patients were over three years of age at the time of death, and the diagnosis was proved by autopsy in each instance.

By fourteen years, 14 per cent died of their heart lesion.

By thirty years, 50 per cent died of their heart lesion.

By forty-one years, 71 per cent died of their heart lesion.

In analyzing the causes of death in these cases, 18, or 23 per cent, died of congestive heart failure.

5, or 6 per cent, died of rupture of the ductus or left ventricular failure.

42, or 53 per cent, died of bacterial endocarditis.

4, or 5 per cent, died of an associated cause of death in which the cardiac state was contributory.

Maude Abbott^{8, 10} found the incidence of subacute endocarditis to be 25 per cent. Gross¹¹ regards it as 20 to 25 per cent.

The hazards of the patent ductus arteriosus are cardiac decompensation (prognosis here when untreated is probably directly related to the size of the opening), bacterial endocarditis or endarteritis, aneurysmal dilatation of the ductus,¹² rupture of the ductus,⁹ and possibly retrograde thrombosis with release of emboli to various parts of the body.

DIAGNOSIS

During the first three to four years of life, the patent ductus arteriosus is seldom recognized. In some cases, during an incidental physical examination, the murmur may be heard, and the child may be given the "waste-basket diagnosis" of congenital heart disease. When the child progresses to the period of increasing exercise, symptoms of dyspnea, increased heart rate, or a pounding heart may develop. Some patients complain of a buzz or a hum in the chest. Decompensation is unusual in children. Cyanosis is present only as a terminal symptom of impending death. As a result of pressure on the recurrent nerve, hoarseness may be present. According to Gross, the lesion is more frequently found in females than in males.

The physical findings boil down to a few important signs and numerous subsidiary signs of confirmatory evidence. Probably the most important single sign is a continuous coarse machinery murmur found at the pulmonic area in the second or third interspace to the left of the sternum. The murmur is accentuated in systole. It is transmitted to the pericardium and to the axillae, especially the left axilla. It is often heard over the back, and is diminished over the neck vessels. A palpable thrill often accompanies the murmurs. According to Bullock, Jones, and Dolley,¹³ when infants and patients with cyanosis are excluded, such a murmur is the strongest evidence for the presence of a patent ductus arteriosus without other congenital defects which would contraindicate operation. Patients with multiple defects rarely survive infancy. Cases with aortic or pulmonary atresia, where the ductus acts as a compensatory mechanism, show cyanosis. Defects, such as a patent interventricular septum, a patent foramen ovale, or a bicuspid aortic valve may exist under the conditions mentioned, but they would not change the indication for operation. Coarctation of the aorta should be carefully ruled out. A second sign of importance is the blood pres-

sure. The systolic level is normal or slightly lowered, while the diastolic level is greatly decreased. With the high pulse pressure, the Corrigan pulse and the pistol-shot sounds may be detected in the peripheral arteries. An appreciable number of patients are below par in weight and physical development, although they are mentally alert.

Inspection may show visible pulsation with increased thrust. Percussion shows a heart of normal or slightly increased size. The laboratory data are not remarkable. The electrocardiogram is normal, a point of differentiation from pulmonary stenosis which shows right axis deviation.

The x-ray findings are not diagnostic, but they serve as important contributory evidence. They also bear witness as to the effectiveness of surgical therapy.⁶ In roentgenograms, kymograms, and fluoroscopy, one should look for the following:

1. A possible enlarged left ventricle.
2. Increased pulsation of the left ventricle and the pulmonary artery.
3. Unusual prominence of the pulmonary artery.
4. Engorgement of the pulmonic vessels.
5. Increased pulsations of pulmonary artery branches.
6. Possible dilation of the left auricle.

SELECTION OF CASES

In one of his early papers, Gross⁵ stated the factors which guided him in the selection of cases for operation. In the first place, there should be no associated congenital cardiac defects. A septal opening or a mild (rhenmatic) mitral stenosis are lesions which do not contraindicate operation. In the second place, he believes the patient should show evidence of impaired cardiac function which is unlikely to correct itself by spontaneous closure. To meet the second requirement, the patient must be observed over a period of time. In addition, there should be the assurance that a patent ductus exists as evidenced by the presence of a characteristic murmur, thrill, blood pressure, and x-ray signs as stated.

Gross also stated that the operation should not be done in the presence of bacterial endocarditis. Touroff and Vessell,¹⁴ feeling that ligation of the ductus might benefit the patient with a patent ductus who also had endocarditis, operated upon four cases. Operation in the first case was successful and the patient remained cured for thirty-six weeks, at which time the paper was published. The second patient succumbed to the disease, and the third and fourth patients died of hemorrhage on the table.

OPERATION

R. E. Gross, of Boston, deserves and unquestionably will receive lasting recognition for his excellent work in devising an efficient operative method for ligation of the ductus arteriosus. The careful work of Gross

and his colleagues, the thoroughness of investigations, the manner with which all presentations are made, and the strict selection of cases distinguish all their presentations.^{5, 11, 15, 16}

Munro,¹⁷ in 1907, first suggested the possibility of ligating the ductus arteriosus, advocating a transsternal approach. According to Gross, O'Shaughnessy¹⁸ was the first to make the attempt, but it was not successful. Strieder¹⁹ made the next attempt in a patient who had subacute bacterial endocarditis, but obliteration of the vessel could not be achieved. It remained for Gross to be the first to perform the operation successfully.

Some of the operative complications are as follows:

1. Hemorrhage from the ductus during dissection.
2. Sepsis.
3. Pneumonia.
4. Inability to identify the duct.
5. Incomplete occlusion of the duct.
6. Perforation of the duct by erosion from the ligature.
7. Injury to the recurrent laryngeal nerve. (This, however, would not be an important matter because the larynx would readily accommodate itself to the injury of this nerve.)
8. Postoperative thrombus.

Postoperatively, Gross observed a cessation of the thrill, disappearance of the murmur (except in a few early cases where the single ligature apparently was not placed tightly enough, and residual murmurs were found), a definite rise of diastolic blood pressure, a diminished cardiac activity, a gain in weight and strength in the retarded children; a return of the cardiothoracic ratio to normal, and cessation of bouts of cardiac failure in two patients who exhibited them preoperatively.

The operative technique of other authors differs from the plan proposed by Gross only in details. Jones and Dolley²¹ also operated on thirteen patients with one fatality. In order to allow serous drainage, the mediastinal pleura is not closed. Pleural effusions are aspirated. They follow the teaching of Mont Reid²² in the selection of ligature material for ligating this large vessel, and recommend an umbilical tape ligature of woven silk $\frac{3}{32}$ of an inch in width. More recently, Gross has been supplementing the ligation of the vessel by means of woven silk with a ligature of cellophane, weight 300, of the unsurfaced type. Herman Pearce, of Rochester, N. Y., has shown by experimental work that cellophane markedly increases the proliferation of fibrous tissue of a vessel so treated. These authors point to Holman's work²³ on arterio-venous fistula where he showed that the obliteration of such a fistula causes an automatic rise of blood volume in the arterial tree. Hence, they feel that postoperative infusions and transfusions should not be used. Their one fatality was a case of postligation thrombus.

CASE REPORT

The patient D. F., a girl aged 15 years, was first admitted to the Santa Rosa Hospital, San Antonio, Texas, May 6, 1941, on the medical service of Dr. Merton M. Minter. Her complaints on admission were cough, headache, weakness, and dyspnea at all times.

Present Illness.—The child was known to have had a heart murmur since the third day of her life. At times she became cyanotic, particularly on marked exertion and after coughing. As a rule she had been able to carry on her usual activities and play, but in the last few years she had gradually noticed more discomfort and respiratory distress. A pounding palpitation had been present as long as she could remember. Her general development had been retarded, more so within the last four or five years. Otherwise, she had been quite well.

Past History.—Previous to the first hospitalization, the patient had measles, chicken pox, and diphtheria. She had no operations and other than the conditions mentioned, she has enjoyed reasonably good health. Menses have not begun.

Physical Examination.—The patient is a pallid, thin, white female of about the stated age of fifteen years. She was somewhat dyspneic and slightly cyanotic. There were no outstanding abnormalities of the head, neck, eyes, ears or throat.

On examination of the chest there was limitation of expansion on the right. The right lung was dull to percussion throughout, with the possibility of fluid at the right base. There was a loud, rough, machinelike murmur in the left second and third interspaces with a palpable thrill. The murmur was audible over the entire precordium, but its greatest intensity was in the left second interspace. The temperature on admission was 101° F.

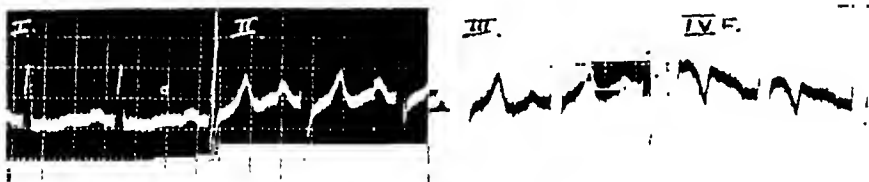


Fig. 1.—Preoperative electrocardiographic tracing. These changes are not characteristic of any definite form of heart disease. Myocardial damage is indicated.

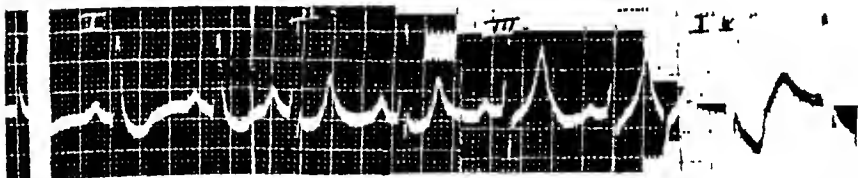


Fig. 2.—Postoperative electrocardiographic tracing. A very mild digitalis reaction is seen. No other changes or abnormalities are noticed which were not present prior to the operation. Note the increase in heart rate.

Laboratory Findings.—The urine showed an acid reaction; the specific gravity was 1.020; there was a trace of albumin; the pus was 1 plus; and there was an occasional red blood cell in the microscopic study. The red blood cell count was 4,350,000; the white blood cell count was 10,350; the differential showed 75 per cent polymorphonuclears, 21 per cent small lymphocytes, 1 eosinophile, 3 transitional cells, and 10 stab forms. The hemoglobin was 84 per cent; the coagulation time was 4.5 minutes.

X-ray of the chest showed congestive changes in each lung with increased density above the hilum in the right lung. The heart shadow was displaced well to the left

so that the apex was one-half inch from the left lateral chest wall. The pulmonary conus showed marked enlargement.

An electrocardiogram taken at this time showed changes not characteristic of any specific heart lesion, but was indicative of cardiac damage.

The patient obviously had an upper respiratory infection plus congestive failure. A diagnosis of patent ductus arteriosus was first made by Dr. Cresswell, and later confirmed by Dr. Merton M. Minter and Dr. Henry N. Leopold. Treatment with sulfathiazole was instituted for the respiratory infection. Digitalis and salyrgan were given for the congestive failure. She improved rapidly under the regime and on May 20, 1941, was able to go home for further rest.

Second Admission.—Patient re-entered the hospital on June 26, 1941, for the purpose of further study and for surgery. The laboratory findings were essentially the same as before except that the white count had fallen to 8,600. The physical examination was the same as before except that the cyanosis and dyspnea were less marked, and the patient was fever free. The blood pressures taken in each arm and each leg were as follows: Right arm, 118/50; left arm, 114/48; right leg, 160/20; left leg, 165/50.

Operation.—The patient was operated on June 24, 1941. She was placed on her back with a small pillow under the left shoulder, and with the left arm placed above her head. Cyclopropane anesthesia was administered by the intratracheal method. An incision was made on the left side of the chest, beginning at the



A.

B.

Fig. 3.—Pre- and postoperative roentgenograms. A. Note enlarged ventricle, prominent pulmonary conus, and congestion of hilus of right lung. B. Note disappearance of the above signs.

lateral border of the sternum and extending laterally to the anterior axillary line over the right second costal interspace. The skin was incised, and the pectoralis muscles were cut in the line of the skin incision. The cartilages of the second and third ribs were cut just medial to the costocartilage junction. The pleural cavity was opened through the second interspace. The lung was collapsed and retracted posteriorly and downward, exposing the pericardium and mediastinum, along which could be seen coursing the phrenic nerve. The mediastinal pleura was picked up gently with fine forceps and was opened through an incision about two inches in length, beginning at the base of the lung and extending upward toward the neck. The fatty areolar tissue was carefully dissected away, exposing the pulmonary artery and the aortic arch. Further dissection exposed the vagus nerve and the

recurrent laryngeal nerve which was picked up and traced medially until it disappeared under the ductus. The thrill at its maximum was found to be over a vessel which extended from the pulmonary artery to the aortic arch, entering the aorta just opposite the left subclavian artery. This structure was four millimeters in diameter and about three millimeters in length. It was carefully freed from the surrounding tissues by blunt dissection until the anterior, medial, and lateral surfaces were freed and thoroughly exposed. When this structure was pressed between the thumb and index finger, the thrill of the heart immediately disappeared. A large aneurysm needle was carefully passed under this structure, separating it from

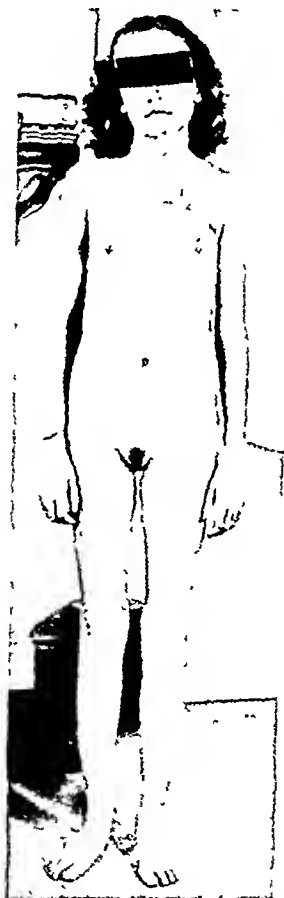


Fig. 4.—Photograph of patient D. F. illustrating her frailness. Note incision in front, left anterior chest.

the right bronchus. The lumen of this vessel was closed by traction on the silk which had been placed around it, and the condition of the patient was observed for a period of four or five minutes. During the time that the vessel was held closed, the blood pressure in the arm rose fifteen points and the patient exhibited no untoward symptoms. When the traction was released, the thrill reappeared in the pulmonary artery and the auricle of the heart, and the blood pressure again dropped. It was felt this was sufficient evident to prove that the structure with which we were dealing was the ductus arteriosus, and it was accordingly doubly ligated with No. 8 braided silk. A small amount of oozing was encountered in the

region of the recurrent laryngeal nerve, but this was controlled by pressure with moist gauze. No effort was made to close the mediastinal pleura because it was felt that if any oozing should occur it would be better to have it enter the thorax rather than to be held in the mediastinum. The lung was then inflated by positive pressure. The cartilage was sutured with No. 32 annealed wire. Two lengths of size No. 30 wire were passed around the second and third ribs, pulling them into apposition with each other. With continuous No. 1 chrome catgut lock sutures, the soft tissues were closed. The skin was closed with a continuous silk lock suture.

Following the operation, the patient was taken to the x-ray room and the chest fluoroscoped. The upper lobe of the lung was well collapsed; the lower lobe, partially collapsed. There was an estimated 300 or 400 cubic centimeters of air just above the diaphragm. The thrill of the heart had entirely disappeared.

Postoperative Course—On the first postoperative day, the pulse was 128, but no murmurs were discernible and the thrill was entirely absent. The patient's respirations were 24. She complained a great deal of pain when awake but was somnolent most of the time. On auscultation, breath sounds were markedly diminished at the left base. Percussion was hyperresonant on the left, indicating the presence of left pneumothorax. An x-ray picture taken at this time revealed the right lung to be relatively clear. There was shown an increased density over most of the left lung extending from the second rib anteriorly to the base. Considerable emphysema was present in the soft tissues surrounding the chest wall. The film made with the patient lying on the right side showed the presence of pneumothorax. The blood pressures taken in each arm and each leg were as follows: Right arm, 125/85; left arm, 125/85; right leg, 135/90; left leg, 120/80.

On the second postoperative day, the patient was very restless and cyanotic most of the day. A thoracentesis was done and 720 cubic centimeters of serous fluid were withdrawn from the left pleural cavity. The following day, the respirations were less labored. The patient was given sulfathiazole for three days as a prophylactic against pneumonia and digitalis postoperatively.

She continued to improve steadily complaining less each day of pain. By July, 1941, she was allowed to sit up a little each day. The wound healed by primary intention. Her temperature, pulse, and respiration were normal. She was dismissed from the hospital on July 7, 1941, with no complaints.

COMMENT

Ligation of a patent ductus arteriosus has undoubtedly been established. Whether it will decrease the incidence of endocarditis is uncertain, especially in view of the postligation infected thrombus cited by Jones, Dolley, and Bullock²¹. In spite of that single case, there seems to be reason to believe that the operation may be successful in this respect. The use of the operation as a curative measure for patients with endocarditis and endarteritis must be regarded as highly experimental, but in view of the relentless course of the untreated disease, further operative undertakings are certainly in order.

REFERENCES

- 1 Patten, B. M.: The Changes in Circulation Following Birth, *Am. Heart J.* 6: 192, 1910.
- 2 Christie, A.: Normal Closing Time of the Foramen Ovale and the Ductus Arteriosus, *Am. J. Dis. Child.* 40: 323, 1930.
- 3 Barclay, A. E., Barcroft, J., Barran, D. H., and Franklin, K. J.: X-ray Studies of the Ductus Arteriosus, *Brit. J. Radiol.* 2: 570, 1928.

4. Barclay, A. E., Barcroft, J., Barran, D. H., and Franklin, K. J.: A Radiographic Demonstration of the Circulation Through the Heart in the Adult and in the Fetus, and the Identification of the Ductus Arteriosus, *Brit. J. Radiol.* 12: 505, 1939.
5. Gross, R. E.: Surgical Management of the Patent Ductus Arteriosus, *Ann. Surg.* 110: 321, 1939.
6. Eppinger, E. C., and Burwell, C. S.: The Mechanical Effects of a Patent Ductus Arteriosus on the Heart, *J. A. M. A.* 115: 1262, 1940.
7. Eppinger, E. C., Burwell, C. S., and Gross, R. E.: The Effects of the Patent Ductus Arteriosus on the Circulation, *J. Clin. Investigation* 20: 127, 1941.
8. Abbott, Maude: Persistent Patency of the Ductus Arteriosus, *Nelson's Loose-Leaf Medicine* 4: 266, 1937.
9. Jones, J. C., Dolley, F. S., and Bullock, L. T.: The Diagnosis and Surgical Therapy of Patent Ductus Arteriosus, *J. Thoracic Surg.* 9: 413, 1940.
10. Abbott, Maude: Atlas of Congenital Heart Disease, New York, 1936, American Heart Association, pp. 60-61.
11. Gross, R. E.: Surgical Closure of the Patent Ductus Arteriosus, *J. Pediat.* 17: 716, 1940.
12. Graham, E. A.: Aneurysm of the Ductus Arteriosus, With a Consideration of Its Importance to the Thoracic Surgeon, *Arch. Surg.* 41: 324, 1940.
13. Bullock, L. T., Jones, J. C., and Dolley, F. S.: The Diagnosis and the Effects of Ligation of the Patent Ductus Arteriosus, *J. Pediat.* 15: 786, 1939.
14. Touroff, A. S. W., and Vessell, H.: Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus, *J. Thoracic Surg.* 10: 59, 1940.
15. Gross, R. E., and Hubbard, J. P.: Surgical Ligation of the Patent Ductus Arteriosus; Report of the First Successful Case, *J. A. M. A.* 112: 729, 1939.
16. Gross, R. E.: A Surgical Approach for Ligation of a Patent Ductus Arteriosus, *New England J. Med.* 220: 510, 1939.
17. Munro, J. C.: Ligation of Ductus Arteriosus, *Ann. Surg.* 46: 335, 1907.
18. O'Shaughnessy, Laurence: By personal communication to Gross, reference No. 11 above.
19. Strieder, J. W.: Discussion of paper by Touroff and Vessell, *J. Thoracic Surg.* 10: 80, 1940.
20. Graybiel, A., Strieder, J. W., and Boyer, N. H.: An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient With Subacute Bacterial Endocarditis, *Am. Heart J.* 15: 621, 1938.
21. Jones, J. C., Dolley, F. S., and Bullock, L. T.: The Diagnosis and Surgical Therapy of a Patent Ductus Arteriosus, *J. Thoracic Surg.* 9: 413, 1940.
22. Reid, Mont: The Ligation of Large Arteries, *Surg., Gynec. & Obst.* 58: 287, 1934.
23. Holman, Emile: Certain Types of Congenital Heart Disease Interpreted as Intracardiac Arteriovenous and Venoarterial Fistulae, Patent Ductus Arteriosus, *Bull. Johns Hopkins Hosp.* 36: 61, 1925.

ANTERIOR DISLOCATION OF THE DISTAL EXTREMITY OF THE ULNA

REPORT OF A CASE

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AN ANTERIOR dislocation of the distal extremity of the ulna is undoubtedly a rare lesion, yet the distinctive mechanics of its production and the peculiar local pathologic changes make it an extremely interesting one. A report of the findings in a recently treated case was considered worth while.

CASE REPORT

A. A., colored female, aged 37 years. On Aug. 3, 1941, the patient was riding in a car which turned over. The dorsum of the forearm was on the ground, and the side of the car came down upon the flexor surface. Quite a bit of straining and twisting were necessary for the patient to disengage the arm. The patient had immediate pain and swelling at the wrist, with inability to use the wrist without increasing the local pain. She was brought to the hospital. X rays were taken and reported as negative, hence the patient was told to apply hot soaks and to rest the extremity at home.

Three weeks later the patient returned to the hospital complaining of persistent throbbing pain in the right wrist. The pain became quite sharp with any attempted wrist motion or hand flexion. The pain was always referred to the volar aspect of the wrist. The swelling locally was most marked at this point but also extended distally to the finger tips and proximally to the midforearm.

On examination there was marked swelling of the whole distal third of the forearm, extending onto the hand. Point tenderness was localized over the volar aspect of the distal radioulnar joint. The distal extremity of the ulna was palpable in its dislocated position over the volar aspect of the wrist. Review of the x ray films (Fig. 1a and b) taken at the date of original examination three weeks previously showed the anterior dislocation of the ulna with a fracture of the ulna styloid process. Motions at that time were

Wrist:	RIGHT	LEFT
Flexion	15°	80°
Extension	35°	90°
Supination	From 15° to 80°	90°
Pronation	0°	90°
Fingers:		
Flexion	50%	100%
Extension	90%	100%

On Aug. 23, 1941, an open reduction was done. The incision was made transversely across the wrist joint to the ulnar styloid and extended cephalad for a distance of approximately two inches (Fig. 2a). The skin flap was retracted, and

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dissection carried down along the edge of the flexor digitorum profundus, to the anterior aspect of the wrist joint. The distal extremity of the ulna was found lying upon the anterior aspect of the radius and displaced almost 1 cm. toward the radial side of the wrist. This displacement was firmly fixed by the contracted pronator quadratus muscle (Fig. 2*b*). The capsule of the wrist joint was opened transversely to expose this area for inspection. The triangular ligament and the detached ulnar styloid remained in their normal positions firmly attached to the

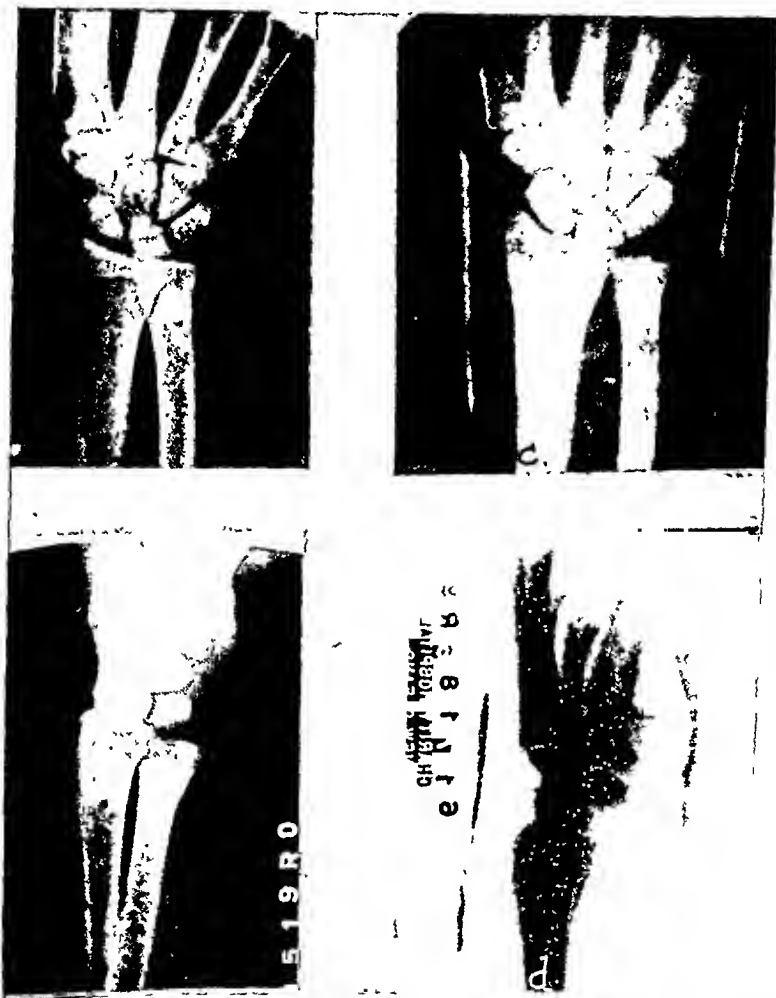


Fig. 1.—*a*, Typical displacement of ulna toward radial styloid process *b* Typical anterior displacement when true lateral x-ray projection is made *c*, Anteroposterior view after reduction. *d* Lateral view postreduction.

capsule, and could not be displaced when grasped with a forceps. No damage had occurred to the articular cartilage of the radius or ulna at the distal radioulnar joint. Following incision of the capsule and complete exposure of the radioulnar joint, a periosteal elevator was inserted as a lever and an attempt made to reduce forcibly the dislocated ulna. Even with strong force this could not be accomplished. The origin of the pronator quadratus was released from the lower one and one-half inches of the ulna, and immediately the dislocation could be reduced using an elevator

as a lever. Full pronation and supination could be demonstrated once this was done. The origin of the pronator quadratus was reattached and a capsulorrhaphy done to reinforce the support on the anterior aspect of the distal radioulnar joint.

The wrist and elbow were immobilized in a plaster of Paris splint maintaining the forearm in full supination, and held in this position for three weeks. Physiotherapy in the form of whirlpool baths, massage, and graduated exercise was continued for an additional three-week period.

At date of the last examination Nov. 21, 1941, the patient had resumed full activity as a housewife and maid, using the wrist and hand without disability, except for a sensation of slight stiffness in the wrist with full supination. Motions at this time were

Wrist:	Pronation	50°
	Supination	90°
	Extension	90°
	Flexion	45°

Full range of finger motion.

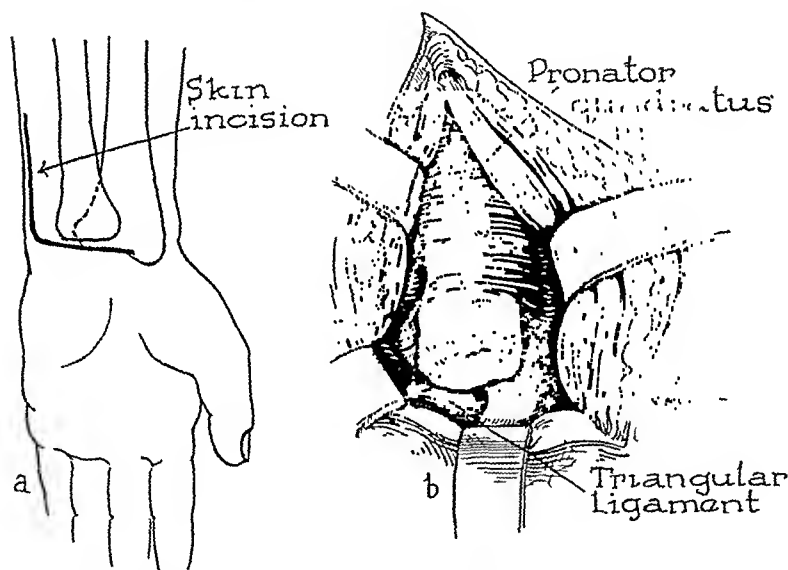


Fig. 2.—a. Outline of skin incision used. b. Drawing at operation showing deforming effect of pronator quadratus muscle, also intact undisplaced triangular ligament.

DISCUSSION

Uncomplicated anterior dislocation of the ulna was described for the first time by P. Desault in 1791 as an incidental finding on a cadaver. A complete description of the mechanics and a discussion of the immediate care were published by Cotton and Brickley in 1912¹ together with a résumé of 27 cases reported in the literature, in which résumé the exact mechanism of production of the dislocation is recorded. As a result of their investigations Cotton and Brickley felt that there were at least two mechanisms by which this lesion could be produced: (1) forced supination and (2) direct backward force on the hand with the ulna fixed mechanically or by force of triceps mechanism. There

is no evidence to dispute their conclusions. An interest in the lesion was aroused for a short time,²⁻⁴ yet no description of the mechanics of the production of an anterior dislocation of the ulna, or of its aftercare has been included in any of the recent literature. In 1937 Vergoz and Choussat⁵ reported sixty-eight cases compiled from the literature, but not including any of those reported in this country. Their report however is concerned with the reconstruction procedure used in the care of an old unreduced dislocation of the ulna.

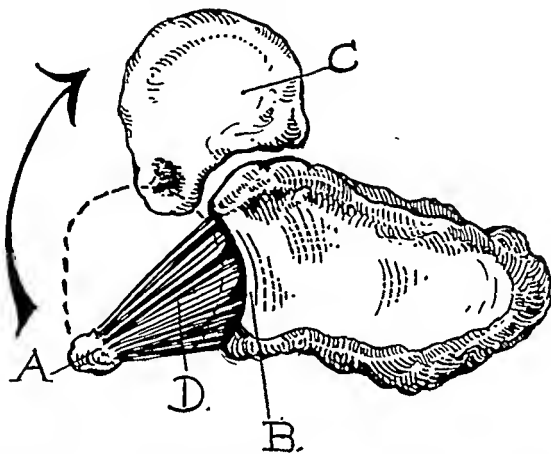


Fig. 3.—A. Styloid process of ulna. B. Attachment of triangular ligament to radius. C. Shaft of ulna displaced anteriorly and impinging upon volar aspect of radius. D. Triangular ligament.

Probably anterior dislocation of the ulna is always associated with either a fracture of the ulnar styloid or a tear of the triangular ligament at its point of insertion into the styloid process. When seen early before spasmodic contracture of the pronator quadratus muscle has occurred, reduction of an anterior dislocation of the ulna should be easily accomplished. The main force resisting reduction is the pull of the pronator quadratus. Where the interosseous membrane is not torn the displacement of the ulna may become mechanically fixed on the anterior aspect of the radius (Fig. 3). Traction against this force manually would be made much more effective with the administration of general anesthesia, or regional block anesthesia. In the more resistant cases, either skeletal traction exerted on the ulna itself or the use of a lever inserted between the radius and the ulna might be utilized with effect.

Where the dislocation has been allowed to remain for a period of time sufficient to allow cellular infiltration and fibrosis within the substance of the pronator quadratus muscle to occur, open reduction becomes necessary. Early simple open reduction followed by a capsulorraphy gives a satisfactory result. Later a more radical procedure must be done because of the organization which has developed in the distal

radioulnar joint. Sauvé and Kapandji⁶ advise the production of a pseudoarthrosis in the ulna at the level of the distal third with replacement of the head of the ulna in its normal relationship with the radius, so as to allow free pronation and supination, yet prevent ulnar deviation of the hand at the wrist. Resection of the distal extremity of the ulna as advised by Darrach³ would give a perfectly satisfactory result.

The disturbance in function of the flexors and extensors of the hand associated with this type of dislocation is sufficiently severe that emphasis must be laid upon the importance of reduction at the earliest possible moment.

REFERENCES

1. Cotton, F. J., and Brickley, W. J.: Luxation of the Ulna Forward at the Wrist (Without Fracture), *Ann. Surg.* 55: 368, 1912.
2. Hitzrot, James M.: Anterior Dislocation of the Lower of the Ulna. Late Result, *Ann. Surg.* 55: 623, 1912.
3. Darrach, William: Anterior Dislocation of the Head of the Ulna, *Ann. Surg.* 56: 802, 1912.
4. Darrach, William: Habitual Forward Dislocation of the Head of the Ulna, *Ann. Surg.* 57: 928, 1913.
5. Vergoz and Choussat: Luxation palmaire isolée de l'extrémité inférieure du cubitus, traitée par la nouvelle technique de Sauvé et Kapandji, *Mem. Acad. de chir.* 63: 992, 1937.
6. Sauvé and Kapandji: Nouvelle technique de traitement chirurgical des luxations récidivantes isolées de l'extrémité inférieure du cubitus, *J. de chir.* 47: 589, 1936.

GROSS PATHOLOGIC ANATOMY OF THE UNUSUAL SHOULDER SPECIMENS IN TWO HUMAN CADAVERS, WITH SOME REMARKS RELATIVE TO THE SURGICAL SIGNIFICANCE OF THESE FINDINGS

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UNREDUCED ANTERIOR SUBCLAVICULAR DISLOCATION OF THE HEAD OF THE HUMERUS OF TWO YEARS' DURATION

THIS shoulder joint specimen is noteworthy because of the following features:

1. The anatomic relations of the dislocated humeral head, and the pathologic changes in the bones and soft tissues of the old and new articulations are defined.
2. The relative margin of safety to the adjacent vessels and nerves, and the functional integrity of the neurothrosis are emphasized.
3. The anatomic findings in this specimen of only two years' duration indicate that surgery of considerable magnitude would have been necessary to mobilize and reduce the dislocated humeral head, and that if reduction had been successful, in view of the advanced degenerative changes involving the humeral head and glenoid fossa, any procedure other than a resection of the humeral head or an arthrodesis of the shoulder joint might have proved inadequate. Indeed, the functional efficiency of the new shoulder joint, as was gathered from the history of the patient and as may be interpreted from the anatomic findings, might have made the wisdom of operative interference in this case questionable.

GROSS ANATOMIC FINDINGS

The specimen was obtained from the cadaver of a white female, aged 39 years, whose death had been due to a malignant lesion of the large intestine with metastases. She had sustained a traumatic dislocation of the right shoulder joint two years prior to her death, that had remained uncorrected after several attempts at closed reduction had failed.

Right Shoulder Region.—The undissected right upper extremity could be abducted at the shoulder to 45° , internally and externally rotated 45° each, and flexed and extended 45° each.

Muscles: The deltoid muscle was well developed and overlay the empty glenoid cavity. The coracobrachialis, short head of the biceps, and pectoralis minor muscles, arising from the coracoid process, stretched

across the humeral head anteriorly. The teres major and pectoralis major muscles were attached to the margins of the bicipital groove and merged with the thick capsule enveloping the humeral head. The subscapularis lay below and anterior to the head and retained its insertion to the lesser tubercle. The long head of the triceps muscle was attached to the infraglenoidal tubercle. The combined tendons of the supraspinatus, infraspinatus and teres minor muscles (the musculotendinous cuff) overlay and terminated in the soft tissues filling the old glenoid cavity, having become completely detached from the greater tubercle.



Fig. 1—Anteroposterior roentgenographic view of the right shoulder region of Cadaver 1. The head of the humerus (*h.h.*) is displaced to a position anterior to the scapula (*s*), medial to the glenoid fossa (*g.f.*) and the coracoid process (*c.p.*), and inferior to the middle third of the clavicle (*cl.*). There is marked decalcification of the bones. The articular surface of the humeral head is well defined, regular, and convex in its inner two-thirds, while its outer one-third is irregular and flattened.

Vessels and Nerves: The axillary vessels and brachial nerve plexus were deflected medialward and were angulated over the medial aspect of the humeral head. These structures were not visibly flattened or compressed and they presented no gross histologic changes in the region of the dislocated humeral head. The lumina of the vessels were patent, the arteries were well injected, and there were no varicosities. All of the muscles of the right shoulder, arm, forearm, and hand were as well developed as those on the left side, indicating the integrity of the nerve plexus during life.

The Nearthrosis: The humeral head was dislocated to a position anterior to the scapula, medial to the coracoid process and beneath the

middle third of the clavicle (Figs. 1 and 2). The head of the humerus was covered by a thick capsule, measuring 3 to 4 mm. in thickness, that was adherent to the anterior surface of the scapular neck and that was attached, laterally, to the medial margin of the hypertrophied coracoid process. The anterior, medial, and inferior portions of the capsule were inseparable from the overlying muscles. The capsule was opened by severing its coracoid attachment. Its inner surface was shiny and smooth and its cavity contained about 5 c.c. of yellow, mucoid fluid. It was somewhat fibrillated in the region of the lesser tubercle. The new joint cavity was completely closed and had no connection with the original glenoid cavity (Figs. 2 and 3). Microscopically, the lining of this new capsule was composed of one or more layers of flattened, modified connective tissue cells (Fig. 4).



Fig. 2.—The right shoulder specimen of Cadaver 1, viewed anteriorly. The dislocated humeral head (*h.h.*) has been exposed by severing the overlying thick capsule (*c.*) at its attachment to the hypertrophied coracoid process (*c.p.*). This capsule has been reflected to expose its shiny articulating surface which is smooth throughout except for some fibrillation in the region of the lesser tubercle (*l.t.*). The cartilage over the medial two-thirds of the humeral head is fairly well preserved, although modified. It is absent over the flattened lateral one-third of the head of the humerus (that portion articulating with the coracoid process), with exposure of the underlying bone which is densified. The greater tubercle (*g.t.*) is smooth and without tendinous attachments, and the bicipital groove is shallow. The acromioclavicular joint (*ac.jt.*) shows advanced degeneration of its fibrocartilaginous tissues.

Coracoid Process: This was hypertrophied and presented on its medial aspect two facets, one posterosuperiorly and the other antero-inferiorly, that were smooth and eburnated and that articulated with the lateral portion of the humeral head (Figs. 2, 3 and 6).

Humeral Head: This was hypertrophied and approximately one-third larger than the head of the left humerus. Its medial two-thirds

was covered with thin, irregular and degenerated cartilage, while its lateral one-third was denuded of all cartilage with exposure of the eburnated subchondral bone. The humeral head was flattened considerably in its posterolateral portion and this region of the head articulated with an area on the anterior surface of the scapular neck, just medial to the glenoid fossa, that was elevated and relatively smooth, but the periphery of which was quite irregular, especially inferiorly and medially where the proliferative bone formed actual ledges. The thin posterior portion of the capsule was interposed between the humeral



Fig. 3.—The right shoulder specimen of Cadaver 1, viewed from above. The humeral head (h.h.) has been rotated from its position in order to expose the new shoulder joint cavity. The internal surface of the thickened capsule (c.) of this closed cavity is smooth and shiny. The features of the humeral articular surface are well demonstrated from above. The medial two-thirds are covered with thin, modified hyaline cartilage, and the outer one-third (that portion articulating with the coracoid process c.p.) is rough, irregular, and denuded of cartilage with exposure of the subchondral bone. There is considerable flattening of the posterolateral portion of the humeral head, which area had articulated with the anterior surface of the scapular neck. The degenerated cartilage of the articular surface of the resected clavicle (cl.) is demonstrated.

head and the modified anterior surface of the scapular neck. The greater tubercle was smooth and without tendinous attachments. The medial and lateral borders of the bicipital groove were less pronounced and the bicipital sulcus was more shallow in the right humerus than in the left humerus (Figs. 2, 3 and 6).

Glenoid Cavity: This was shallow and diminished in its antero-posterior dimensions, due possibly to fracture and displacement of the anterior lip of the fossa at the time of dislocation. The glenoidal labrum and the joint cartilage were absent, and the glenoid cavity was filled with soft tissue and the terminal portion of the musculotendinous cuff. The tendon of the long head of the biceps brachii muscle was intact and stretched from its attachment to the supraglenoidal tubercle, across the glenoid fossa to enter the bicipital groove about 4 cm. below the tubercles. The cavity of its sheath had no connection with the new shoulder joint cavity, but communicated at its posterior extremity through a small opening with the glenoid fossa (Fig. 5).

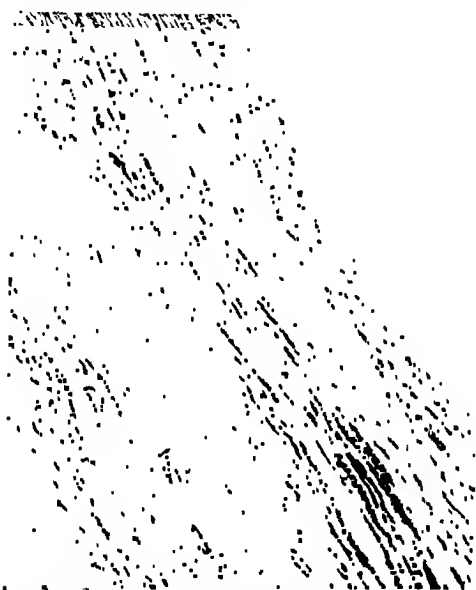


Fig. 4.—Photomicrograph ($\times 50$) of a section of the capsule from the new shoulder joint of Cadaver 1. The articulating surface is lined by flattened, modified connective tissue cells, supported by compacted connective tissue and muscle fibers.

Scapula: This was lighter in weight than the left scapula, despite the excessive proliferation of bone in the region of the glenoid cavity, acromion and coracoid processes, and scapular neck. The body of the scapula was thin and transparent. There was considerable atrophy of the cancellous and cortical bone of the head, neck, and shaft of the right humerus (Fig. 6).

Other Articulations.—Advanced degenerative changes were present in the left (undislocated) shoulder joint, both acromioclavicular joints, both knee joints, both elbow joints, and the spine.

Left Shoulder Joint: There was a complete circular defect (2 cm. in diameter) in the musculotendinous cuff, with marked fibrillation of the deep surface of the remaining portions of the cuff. The long bicipital

tendon was considerably frayed and degenerated and had become detached from the supraglenoidal tubercle. The cartilage of the glenoid fossa and humeral head was thinned and fibrillated, and in areas it was absent with exposure of the underlying subchondral bone. The margins of the glenoid cavity and the humeral head were irregular due to bony proliferative and regressive changes (Fig. 7).

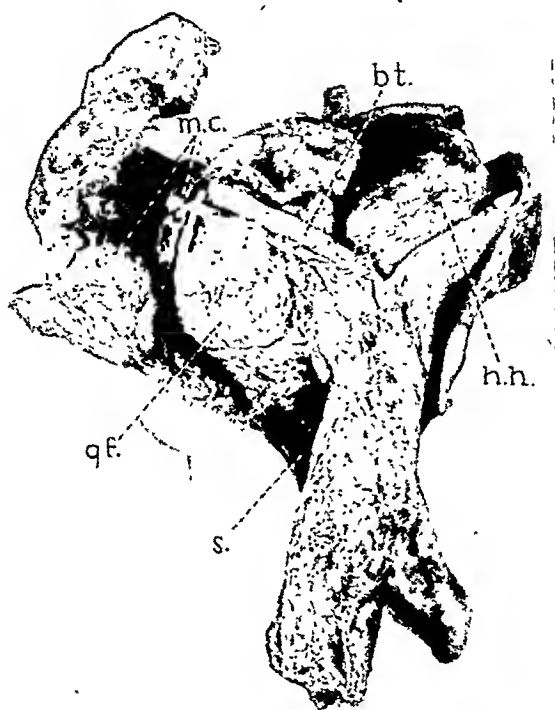


Fig. 5—Lateral view of the right shoulder specimen of Cadaver 1. The long bicipital tendon (*bt.*) is intact and extends, within its own sheath, from the supraglenoidal tubercle to enter the bicipital groove of the humerus about 4 cm. below the tubercle. The cavity of the sheath is closed except for a small posterior communication with the glenoid fossa (indicated by marker). The musculotendinous cuff (*m.c.*), which terminated in the soft tissues filling and overlying the glenoid fossa (*qf.*), has been cut away to expose the contents of the latter. The position of the humeral head (*h.h.*) and shaft anterior to the scapula (*s.*) is well demonstrated.

DISCUSSION

Specimens of anterior dislocation of the humeral head have been described by Flower,¹ Broca and Hartman,² Delbet,³ Pascalis and Monod,⁴ Amabilis,⁵ Petit-Dutaillis,⁶ and Fumek-Brentano.⁷ These authors have stressed certain features which are well demonstrated in the specimen herein described: the flattened posterior portion of the enlarged head which articulates with the scapula and the inferior surface of the coracoid process; the formation of a new "glenoid fossa" on the anterior surface of the neck of the scapula; the new capsule enveloping the head,

that is formed, in part, from the deep surface of the subscapularis muscle, and that is reinforced, posteriorly, by the tendons of the short rotator muscles; the occasional ossified bodies within the tendons of the subscapularis and infraspinatus muscles, that articulate with the humeral head; the displaced tendon of the long head of the biceps muscle, and the contracted subscapularis muscle, both of which interfere with mobilization of the dislocated humeral head. In these descriptions, the axillary neurovascular structures were usually situated medial to the head of the humerus, although in the case of Funk-Brentano⁷ they lay external to the head and within a gutter formed in a bony plaque



Fig. 6.—The macerated bones at A are those from the dislocated shoulder joint specimen of Cadaver 1, and those at B are for comparison and were removed from the grossly normal shoulder joint of a 44-year-old colored female.

1, Cephalic view of the acromial end of the clavicle; 2, anterior view of the scapula; 3, cephalic view of the humeral head; 4, cephalic view of a transection of the shaft 4 cm. below the anatomic neck.

A-1 demonstrates marginal proliferation at the acromial end of the clavicular segment. A-2 demonstrates irregular bony proliferation involving the acromion process, the coracoid process, and the anterior surface of the scapular neck at the site of the new "glenoid fossa." There are two articular facets on the inferomedial surface of the hypertrophied coracoid process. The body of the scapula is thin and atrophic. A-3 shows the flattening of the posterolateral surface of the dislocated humeral head, the irregularity of the subchondral bone, especially in the lateral one-third, and the regression of the greater and lesser tubercles. A-4 demonstrates the advanced atrophy of the cortical and cancellous bone in the region of the humeral shaft, with relative enlargement of the marrow cavity.

within the subscapularis muscle. Atrophy of the deltoid muscle, indicative either of injury to the circumflex nerve or of disuse, was an occasional feature.

In some of these complete shoulder specimens and in many of the humeral heads resected by surgeons in the past for the correction of

recurring dislocation, a grooved defect, or, less often, a simple flattening was observed on the posterolateral surface of the humeral head (Hill and Sachs⁸). This "typical defect" has been observed shortly after a single dislocation and even prior to any attempts at reduction (Eve,⁹ Hermodsson¹⁰), and for this reason it has been interpreted as representing a compression fracture of the spongiosa in this region of the humeral head, caused by the impingement of the posterolateral aspect of the head of

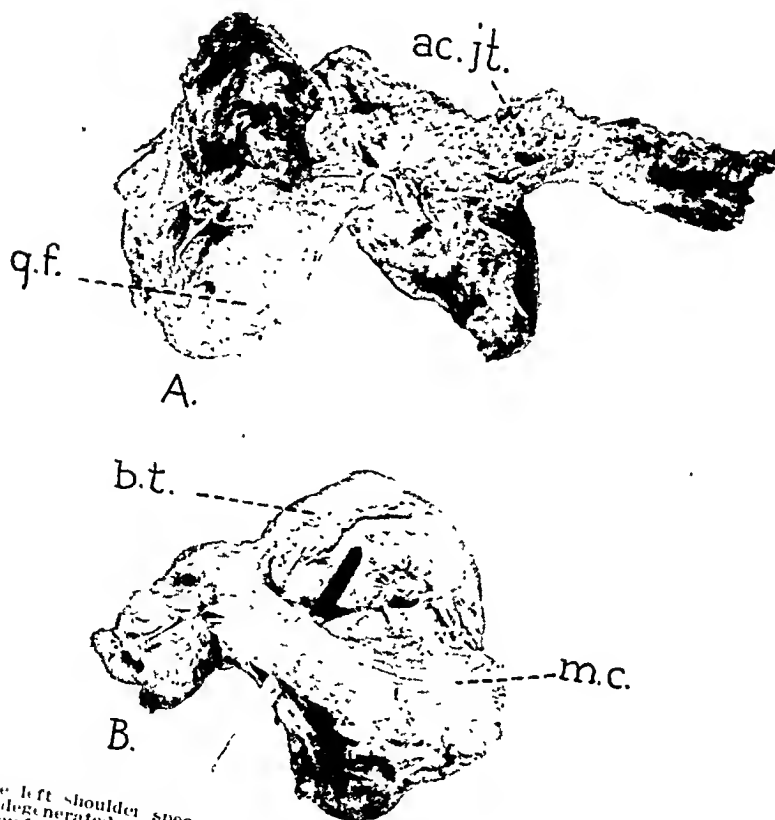


Fig. 7.—The left shoulder specimen of Cadaver 1. A. The glenoid fossa (g.f.) is covered with degenerated cartilage and demonstrates marginal bony proliferation. The articular surfaces of the acromioclavicular joint (ac. jt.) are the site of advanced degenerative changes. B. The musculotendinous cuff (m.c.) has been reflected over the humeral head and it demonstrates a large complete defect (indicated by the marker), and fibrillation of the deep surface. The capital portion of the long bicipital tendon (b.t.) is detached from the supraglenoidal tubercle, flattened, and moderately frayed.

the humerus on the anterior glenoidal rim. It has been suggested that this defect might be an etiologic factor in recurrent dislocation of the humeral head. Although no grooved defect was present on the posterolateral aspect of the head of the humerus in the dislocated specimen here-in described, there was a distinct flattening in this region. While the

evidence was interpreted as favoring the belief that this flattening was attritional in origin, it cannot be denied that it might have represented an area of compression of the humeral head.

The pathologic anatomy in an *acute* anterior (subcoracoid) dislocation consists of the following—the humeral head passes through the anterior and inferior portion of the joint capsule at its glenoidal attachment, often carrying with it the anterior rim of the glenoidal labrum or the anterior lip of the bony fossa, and the margins of the capsular defect envelop the upper humeral shaft. The deltoid muscle and the musculotendinous cuff (short rotators) are stretched across the glenoid cavity and the latter may be avulsed at or near its bony attachments. The humeral head is displaced anterior to the scapula and deep to the subscapularis muscle. The tendon of the long head of the biceps muscle is displaced from the upper portion of the bicipital groove, with or without fracture of the greater tubercle, and it spans the glenoid fossa if it retains, as it often does, its attachment to the supraglenoid tubercle (Key and Conwell¹¹).

In *old* dislocations of the shoulder joint, as indicated in pathologic material and by the experience of those who have operated upon such cases (Codman,¹² Cubbins, Callahan, and Scuderi,¹³ Meng and Miltner,¹⁴ Bennett¹⁵), obstacles to closed or open reduction may be: the contracted and fibrosed subscapularis, pectoralis major and/or latissimus dorsi muscles; the tendon of the long head of the biceps muscle when it lies posterior to the head of the humerus and spans the glenoid cavity; the periarticular fibrous tissues (new capsule and its attachments) which bind the humeral head in its abnormal position; the torn musculotendinous cuff when it overlies and attaches to the soft tissues filling the glenoid fossa; the glenoid cavity, that becomes deformed by marginal bony proliferation and, in some instances, by loss of its anterior lip, and that loses its articular cartilage and becomes filled with scar tissue; the irregular proliferative bony process between the glenoid fossa and the articular surface on the neck of the scapula that receives the displaced humeral head; and the head of the humerus, that becomes hypertrophied and deformed and that loses its articular cartilage. Such changes in the bony, cartilaginous and synovial tissues may interfere with the reconstruction of a satisfactory shoulder joint even following the successful mobilization of the humeral head by division and release of the contracted tissues.

II. ADVANCED DEGENERATIVE DISEASE OF THE SHOULDER JOINT

These shoulder specimens from the same cadaver are noteworthy because of their following features:

1. They represent the most advanced stage of the degenerative processes that may involve this articulation.

2. The character of the degenerative lesions, such as the eburnated articular surfaces and the formation of several nearthroses, indicate that function may be preserved in the presence of advanced degenerative joint disease.

3. The ossified plaques in the deltoid muscle, bilaterally, which served as part of the receptive articular surface for the humeral head, represent bony metaplasia in the muscle and were probably produced by functional forces brought to bear by the humeral head after its erosion through the musculotendinous cuff. The shadow of these bony deposits on the roentgenogram could be misinterpreted for calcifications within the musculotendinous cuff or paratendinous soft tissues (Fig. 8).

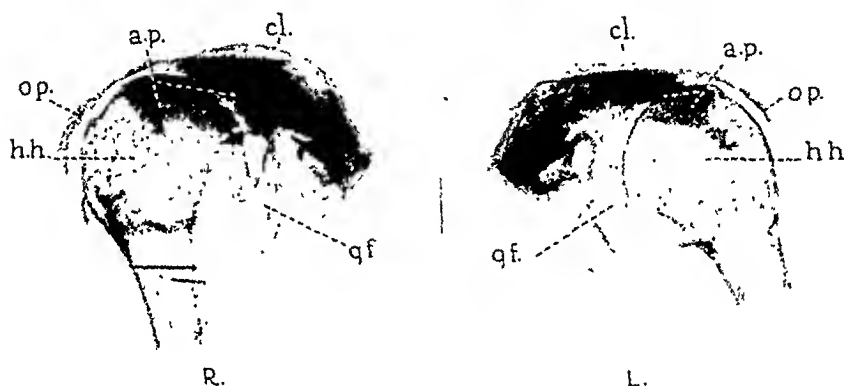


Fig. 8.—Anteroposterior roentgenographic view of the right and left shoulder specimens of Cadaver 2. In both specimens the humeral head (h.h.) articulates with a deep, acetabulum-like socket, made up of an ossified plaque (o.p.) within the deltoid muscle at its acromial attachment, the acromion process (a.p.), the acromial end of the clavicle (cl.), and the glenoid fossa (g.f.).

GROSS ANATOMIC FINDINGS

The specimens were obtained from a colored female, aged 77 years, who had died of bronchopneumonia.

Shoulder Joints.—The advanced degenerative and proliferative changes were similar in the right and left shoulder specimens, but were more marked on the right side.

The humeral head was observed to have eroded completely through the superior portion of the musculotendinous cuff of the shoulder (combined supraspinatus, infraspinatus, teres minor and subscapularis tendons), and only the peripheral attachments of this cuff and of the capsule remained. The humeral head articulated not only with the glenoid fossa but also with broad facets, formed by considerable bony proliferation, on the deep surface of the acromial end of the clavicle and on the deep surface of the acromion process, and with a bony plaque within the

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strated considerable bony proliferation, especially along their articular margins and in the region of the tubercles. This process was more advanced on the right humeral head where the bony proliferation had formed overhanging ledges (Figs. 8, 9, 10 and 11).

The synovia was thickened and in areas demonstrated villus and nodule formations. The deep surface of the deltoid muscle, adjacent to the bony plaque, was markedly fibrillated. The biceps tendon within

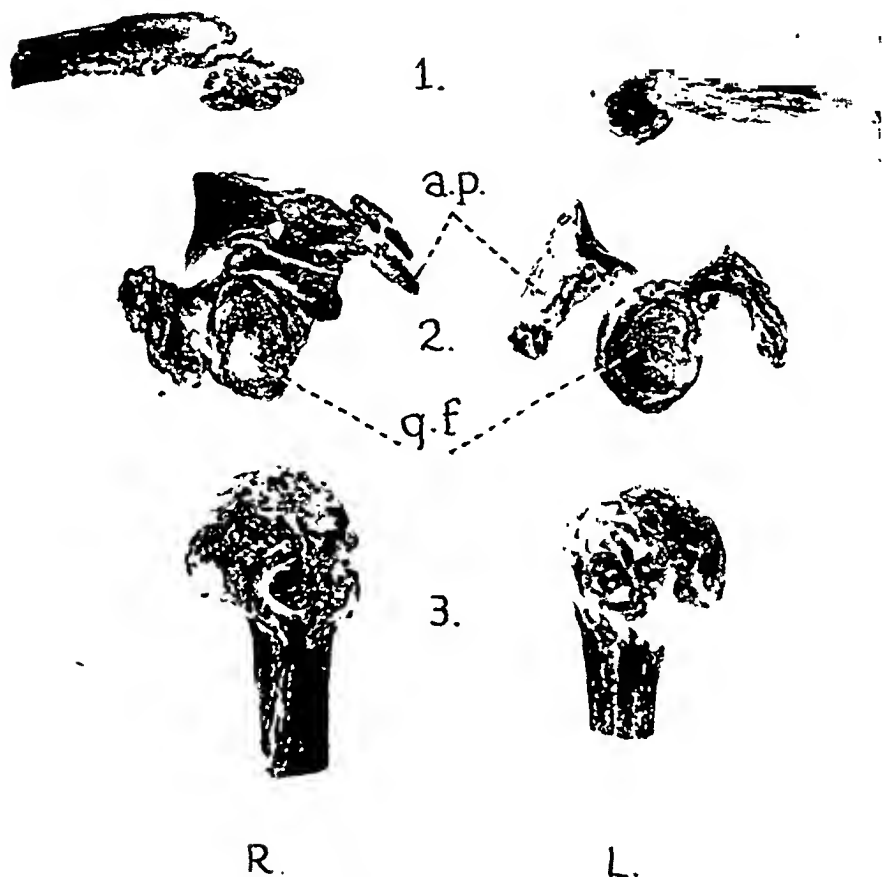


Fig. 10.—Macerated bony components of the right and left shoulder specimens of Cadaver 2. 1. The inferior surface of the acromial end of the clavicle; 2. the glenoid fossa (*g.f.*) and acromion process (*a.p.*), viewed laterally; 3. the humeral head, viewed from above.

In each specimen, there is considerable bony proliferation about the articular facets on the undersurfaces of the acromial end of the clavicle and acromion process, and about the margins of the glenoid fossa. The interval between the acromion process and the superior glenoidal rim in the right specimen is filled with smooth, eburnated bony tissue that presents an incomplete transverse fissure and that acts as part of the extensive articular surface for the reception of the right humeral head. The humeral heads, especially the right, demonstrate marginal bony proliferation and considerable irregularity of the articular surface.

substance of the thinned deltoid muscle at its origin from the acromion process. These four bony surfaces were separated from one another by narrow zones of fibrous tissue, yet their deep, concave surfaces presented one continuous, smooth articular surface for the reception of the humeral head, resembling very much an acetabulum. On the right side only, the normal interval between the glenoid fossa and the acromion process was completely filled with bone and this area was also smooth and eburnated. The cartilage of the glenoid cavity was fibrillated and thinned, and it was absent in the center of the fossa with exposure of the underlying bone. The glenoidal labrum was absent and replaced by marginal bony proliferation, especially anteriorly and posteriorly. The outer half of the humeral head (that is, that part articulating with the acromial end of the clavicle, acromion process, and the deltoid muscle)

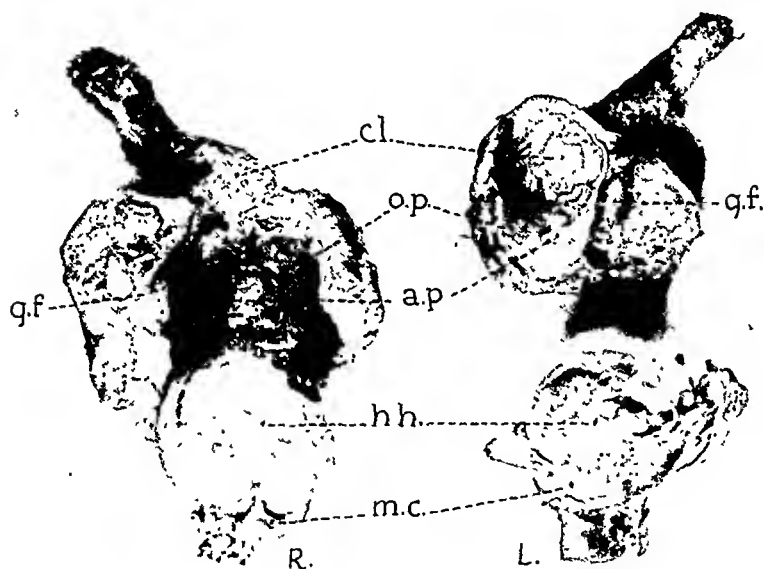


FIG. 9.—The right and left shoulder joints of Cadaver 2 have been opened in order to demonstrate the acetabulum-like sockets with which the degenerated articular surface of the humeral heads had articulated. This deep receptive surface, in both specimens, is composed of the glenoid fossa (*g.f.*), the eburnated undersurfaces of the acromial end of the clavicle (*cl.*) and of the acromion process (*a.p.*), and the ossified plaque (*o.p.*) within the deltoid muscle. Only the peripheral attachments of the musculocapsular cuff (*m.c.*) remain, the humeral head (*h.h.*) having eroded completely through the articular portion of the cuff, so as to articulate directly with the above bony articular surfaces.

was flattened, eburnated in areas, smooth on the left side and very irregular on the right, and showed complete loss of its articular cartilage. The articular cartilage of the medial half of the humeral head (that is, that portion articulating with the glenoid fossa) was preserved but was considerably thinned and fibrillated, and it was absent in small areas with exposure of the subchondral bone. The humeral heads demon-

there is a failure of reparative processes to function adequately. A contributory factor of predisposition has been suggested, that is, that the type of cartilage inherited may be responsible for the earlier and more extensive changes encountered in some individuals (Bauer and Bennett¹⁸). That there may be constitutional factors, such as metabolic disorder or endocrine dysfunction, has been suggested but not proved. Generalized degenerative arthropathies are seen in such a metabolic pigmentary disorder as ochronosis. It has been demonstrated experimentally in laboratory animals that articular cartilage may become modified through the effects of excessive administration of certain hormones (Silberberg and Silberberg¹⁹), and it is possible that the deprivation of such hormones may also exert some deleterious effect on joint structure.



Fig. 12—Histologic preparation ($\times 50$) of a segment of one of the ossified plaques in Fig. 11. This demonstrates adult lamellar bone architecture, with well-formed haversian systems.

The writer has examined most of the articulations of the upper and lower extremities and of the spine of forty-three cadavers, of which forty were male and two female, twenty-six white and seventeen colored, and with ages varying from 22 to 85 years. He has observed that, as a rule, the severity and extent of the degenerative lesions which involved the joints, grossly, were directly proportionate to the age of the subject. The joints involved by degenerative processes in the order of their frequency and severity were: (1) zygapophysial joints of the spine, (2) knee joints, (3) shoulder joints, (4) first metatarsophalangeal joints, (5) acromioclavicular joints, (6) elbow joints, (7) sternoclavicular joints, (8) temporomandibular joints, (9) wrist joints, (10) first metacarpophalangeal joints, (11) hip joints and (12) ankle joints. These

the bicipital groove was frayed and flattened and it was attached to the bone at the proximal end of the bicipital sulcus, its capital portion being absent.

The oval-shaped plaques within the deltoid muscle measured 46 mm. in length, 22 mm. in width, and 4 mm. in thickness in the right shoulder specimen, and 26 mm. in length, 18 mm. in width, and 3 mm. in thickness in the left shoulder specimen. Their concave articulating surfaces were smooth and eburnated, while their superficial convex surfaces were irregular and merged with the fibrous and muscular elements of the deltoid (Fig. 11). Histologically, these plaques consisted of compact, adult lamellar bone (Fig. 12).

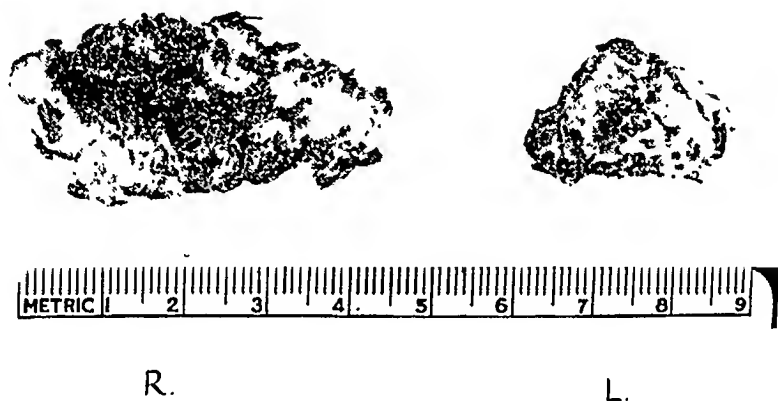


Fig. 11.—The oval-shaped bony plaques from the right and left shoulder specimens of Cadaver 2 are viewed from their deep, articulating side. These surfaces are concave, smooth, and eburnated.

Other Joints.—All of the other articulations in this cadaver showed degenerative changes in the synovia and capsule, and variable proliferative and regressive changes in the osseous structures. These lesions were very advanced in both knee joints, especially on the right side. They were moderately advanced in both acromioclavicular joints, both temporomandibular joints, the left elbow joint, both wrist joints, and in the small joints of the hands and feet, and these lesions were minimal, grossly, in both hip joints, both ankle joints, and the right elbow joint.

DISCUSSION

Degenerative joint disease is the result of wear and tear processes, of advanced age, and of repeated trauma which may be caused in a variety of ways. It has no relation to specific or nonspecific inflammatory processes. There is evidence to support Meyer's hypothesis of attrition,^{16, 17} namely, that in addition to trauma and long-continued use

matory reaction is initiated by their extrusion into an adjacent bursa or tendon sheath. No adequate explanation has been offered to explain the origin of such calcific deposits. In an examination of the microscopic features of specimens removed surgically from thirteen such supraspinatus tendons with calcific deposits, variable degenerative and acute or chronic inflammatory processes were observed in the tendinous and paratendinous tissues. The areas of calcification were situated usually in the densely fibrous, poorly cellular and less vascular regions, and in no instance was there evidence of ossification in association with the calcified deposits. The failure of association of the latter two processes has been observed also in other forms of dystrophic calcification.

Codman¹² stated that he had found no instance of proved ossification of the supraspinatus tendon in his extensive anatomical and clinical material, and he stressed the need for distinguishing bits of tuberosities in the retracted tendons. Meyer¹⁶ apparently also interpreted ossific nodules in the periarticular soft tissues as due to sudden trauma rather than to wear and tear. The ossified plaques in the shoulder specimens described herein, were composed of adult lamellar bone and probably represented bony metaplasia within the deltoid muscle. The humeral heads articulated in part with these areas of ossification, having eroded completely through the joint capsule and the musculotendinous cuff. In the absence of these bony plaques, the humeral heads might very well have eroded through the deltoid muscles and have come to lie subcutaneously. Such extensive stages of destruction must be very rare for they were observed by Meyer¹⁶ only once in about one thousand bodies. That such ossific deposits may occur and that they will throw a shadow on the roentgenogram which is indistinguishable from that of calcifications in the periarticular soft tissues, should be appreciated by surgeons who are utilizing measures such as aspiration, irrigation, needling, or excision, for the removal of calcified deposits in the periarticular structures of the shoulder region.

CONCLUSIONS

1. A consideration of the anatomic and pathologic features in a cadaver specimen of an anterior subclavicular dislocation of the humeral head of two years' duration emphasizes the reasons for failure of attempts at closed reduction and for difficulty of open reduction of the displaced head of the humerus in such cases—the contractural changes in the muscles and other periarticular soft tissues, the interposition of bone and soft-tissue structures, and the modification of the articular components. Because of the marked degenerative changes which involve the bone, cartilage, and synovial tissues, a considerable problem presents itself, if the humeral head is successfully mobilized, in the reconstruction of the shoulder joint, in the restoration of its function,

chronic functional lesions occur rather consistently in certain tissues and in certain areas of the same articulation. They have been investigated extensively by Meyer.¹⁷

In an examination of 335 shoulder specimens in 168 human cadavers, the following degenerative lesions have been observed by the writer: changes in the shoulder bursae, bicipital tendon sheath, and joint synovial membrane (thickening of the walls, fraying, villus and nodule formations, and adhesions); changes in the capsule and musculotendinous cuff (thinning, fraying, fibrillation, partial defects, and complete defects through the entire thickness of the capsule and cuff in 22 specimens or 6.6 per cent); changes in the tendon of the long head of the biceps muscle (flattening, fraying, fibrillation, dislocation and tear); degenerative changes in the articular cartilage of the humerus and glenoid fossa (fibrillation, thinning, denudation with exposure of the subchondral bone which may become polished and eburnated); and proliferative and regressive changes involving the humeral head, tubercles, bicipital groove and glenoid fossa. Meyer¹⁶ has described more advanced stages in the progress of these degenerative processes in the shoulder region: fraying of the deep surface of the deltoid muscle, eventually with complete destruction of a large part of its midportion; partial or total destruction of the articular fibrocartilage and disks of the acromioclavicular joint, and erosion of the inferior capsule of this articulation, with or without joint polishing; formation of a true coracoclavicular articulation; and formation of a joint between the coracoid process and the humeral head and tubercles. The features of the shoulder specimen described in this communication, therefore, represent the degenerative joint lesion in its most advanced form.

In the series of shoulder specimens that I have studied, there was no certain instance, grossly, of calcification in the musculotendinous cuff, although it cannot be denied that roentgenographic and microscopic studies might have uncovered small deposits (Keyes²⁰). Calcific deposits in the supraspinatus tendon were not observed by Sutro and Cohen²¹ in a study of 100 shoulder joints in which changes incidental to senile degeneration were present in the supraspinatus tendon and contiguous structures. Such deposits, however, have been reported by Keyes²⁰ in two specimens in an examination of 192 shoulder joints and by Skinner²² in two instances in a study of 100 shoulder specimens. One may conclude that calcification of the periarticular soft tissues is an uncommon feature in senile degenerative joint disease in the shoulder region.

These remarks are not to be confused with reference to those calcifications in the supraspinatus tendon and in the other short rotators of the shoulder joint that are found usually in younger subjects, not infrequently bilaterally, and that are asymptomatic until an acute inflam-

15. Bennett, G. E.: Old Dislocations of the Shoulder, *J. Bone & Joint Surg.* 18: 594-606, 1936.
16. Meyer, A. W.: Chronic Functional Lesions of the Shoulder, *Arch. Surg.* 35: 646-674, 1937.
17. Meyer, A. W.: Use Destruction in the Human Body, *California & West. Med.* 47: 375-383, 1937.
18. Bauer, W., and Bennett, G. A.: Experimental and Pathological Studies in the Degenerative Type of Arthritis, *J. Bone & Joint Surg.* 18: 1-18, 1936.
19. Silberberg, M., and Silberberg, R.: Action of Estrogen on Skeletal Tissues of Immature Guinea Pigs, *Arch. Path.* 28: 340-360, 1940; The Response of Cartilage and Bone of the Newborn Guinea Pig to Stimulation by Various Hormones (Anterior Hypophyseal Extract, Estrogen, Thyroxin), *Anat. Rec.* 78: 549-558, 1940; Response of Cartilage and Bone of Growing Mice to Testosterone Propionate, *Arch. Path.* 32: 85-95, 1941; The Difference in the Response of Skeletal Tissues to Estrogen in Mice of Various Ages, *Anat. Rec.* 80: 347-367, 1941.
20. Keyes, E. L.: Anatomical Observations on Senile Changes in the Shoulder, *J. Bone & Joint Surg.* 17: 953-960, 1935.
21. Sutro, C. J., and Cohen, L. J.: Basis and Treatment of Calcification of Tendinocapsular Tissues, Especially the Supraspinatus Tendon, *Arch. Surg.* 42: 1065-1071, 1941.
22. Skinner, H. A.: Anatomical Considerations Relative to Rupture of the Supraspinatus Tendon, *J. Bone & Joint Surg.* 19: 137-151, 1937.

and in the prevention of recurrence of the deformity. The recommendation of nonintervention, surgically, in selected cases of dislocation of the humeral head of long duration, where the functional integrity of the nearthrosis is moderately well preserved, is founded on an appreciation of these difficulties.

2. The shoulder specimens in a cadaver with degenerative lesions involving all of the articulations, demonstrate that the advanced stages of degenerative joint disease may be consistent with satisfactory articular function. In these specimens ossified plaques, formed by metaplasia in the deltoid muscle, contributed to the formation of a receptive articular surface for the degenerated humeral head. The shadows of these areas of ossification could be misinterpreted, roentgenographically, for calcifications within the musculotendinous cuff or paratendinous soft tissues of the shoulder region.

REFERENCES

1. Flower, W. H.: On the Pathological Changes Produced in the Shoulder-Joint by Traumatic Dislocation, as Derived From an Examination of All the Specimens Illustrating This Injury in the Museum of London, *Tr. Path. Soc. Lond.* 12: 179-200, 1861.
2. Broca, A., and Hartman, H.: Contribution à l'étude des luxations de l'épaule (luxations dites incomplètes, décollements periostiques, luxations directes et luxations indirectes), *Bull. Soc. anat. de Par.* 65: 312-336, 1890; Contribution à l'étude des luxations de l'épaule (luxations anciennes, luxations récidivantes), *Bull. Soc. anat. de Par.* 65: 416-423, 1890.
3. Delbet, P.: Des luxations anciennes et irréductibles de l'épaule, *Arch. gén. de méd., Par.* 172: 19-39, 144-163, 1893.
4. Pascalis, G., and Monard, R.: Note sur les luxations primitivement irréductible de l'épaule, *Bull. et mém. Soc. anat. de Par.* 88: 296-297, 1913.
5. Amabilis, J.: Contribution à l'étude du Traitement Sanglant des Luxations Anciennes antéro-internes de l'épaule, Thèse de Paris, 1921.
6. Petit-Dutaillis, D.: Note sur une pièce de luxation ancienne de l'épaule, *Bull. et mém. Soc. anat. de Par.* 92: 487-493, 1922.
7. Funck-Brentano, P.: Note sur une pièce de luxation ancienne de l'épaule, *Ann. d'anat. path.* 10: 45-54, 1933.
8. Hill, H. A., and Sachs, M. D.: The Grooved Defect of the Humeral Head. A Frequently Unrecognized Complication of Dislocations of the Shoulder Joint, *Radiology* 35: 690-700, 1940.
9. Eve, F. S.: A Case of Subcoracoid Dislocation of the Humerus With the Formation of an Indentation on the Posterior Surface of the Head, This Joint Being Unopened, With Remarks on the Mode of Production of Fracture of the Anatomical Neck, With Dislocation, *Tr. Med.-Chir.* 63: 317-321, 1880.
10. Hermodsson, I.: Röntgenologische Studien über die traumatischen und habituellen Schultergelenkverrenkungen nach vorn und nach unten, *Acta radiol., Supp.* 20: 1-173, 1934.
11. Key, J. A., and Conwell, H. E.: The Management of Fractures, Dislocations, and Sprains, St. Louis, 1934, The C. V. Mosby Co.
12. Codman, E. A.: The Shoulder. Rupture of the Supraspinatus Tendon and Other Lesions in or About the Subacromial Bursa, Boston, 1934. Privately published.
13. Cubbins, W. R., Callahan, J. C., and Scuderi, C. S.: The Reduction of Old or Irreducible Dislocations of the Shoulder Joint, *Surg., Gynec. & Obst.* 58: 129-135, 1934.
14. Meng, C. W., and Miltner, L. J.: Treatment of Old Dislocations of the Shoulder, *Chinese M. J.* 50: 1161-1172, 1936.

Table I shows the pre- and postoperative data. Each figure is the average of at least three consecutive periods, and is expressed in terms of milligrams per 1.73 sq. M. surface area. DC and IC are the plasma clearances of diodrast and inulin, respectively. D-Tm is the maximal rate of tubular diodrast excretion in milligrams per minute. Whole blood flow data calculated from DC and hematocrit values have been omitted.

Our average normal values⁵ are: DC, 544; IC, 117; D-Tm, 40; $\frac{IC}{DC}$, 0.205; $\frac{DC}{D-Tm}$, 13.56. All of these subjects, therefore, had considerable renal impairment, but none had azotemia. It should be pointed out that only E. A. had an abnormally high $\frac{IC}{DC}$ ratio and that she is the

TABLE I

PATIENT	DATE	DC	IC	D-Tm	IC	DC	BLOOD PRES- SURE
					DC	D-Tm	
P. C., female, aged 50 years	11/14/40	329	63	31.2	0.19	10.54	175/110
	2/13/41			Supradiaphragmatic			
	3/ 7/41	333	59	25.5	0.18	13.05	185/125
	6/ 5/41	342	65	20.7	0.19	16.5	195/130
E. A., female, aged 45 years	1/29/41	180	56	26.6	0.31	6.76	205/120
	2/20/41			Second stage subdiaphragmatic			
	3/ 6/41	241	61	33.3	0.253	7.2	195/120
	6/ 6/41	237	66	36.6	0.28	6.47	180/110
A. G., female, aged 38 years	4/ 6/41	197	55	----	0.28	----	230/140
	5/10/41			Second stage subdiaphragmatic			
	5/21/41	185	50	14.2	0.26	13.0	250/160
H. B., male, aged 50 years	4/30/41	230	59	----	0.25	----	220/130
	5/13/41			Second stage subdiaphragmatic			
	5/22/41	289	68	23.7	0.235	12.2	200/110
S. P., female, aged 35 years	6/23/41	342	74	33.4	0.21	10.2	220/150
	6/30/41			Second stage subdiaphragmatic			
	7/10/41	393	81	47.5	0.20	8.3	210/140

only one whose rate of plasma flow per unit of tubular function, $\frac{DC}{D-Tm}$, fell clearly in the zone of renal ischemia. It was, therefore, probably unreasonable to anticipate postoperative renal hyperemia if ischemia could not be consistently demonstrated preoperatively, but it seems plain that even in this one instance no release of efferent arteriolar spasm took place. DC, IC, and D-Tm apparently increased proportionately after the operation, but the changes were not marked and we are inclined to disregard them.

In patient P. C., the increase in $\frac{DC}{D-Tm}$ tempts one to conclude that hyperemia was produced, but all $\frac{IC}{D-Tm}$ ratios were well within normal limits, DC remained remarkably constant over a period of seven months,

THE EFFECT OF SYMPATHECTOMY ON RENAL BLOOD FLOW IN ESSENTIAL HYPERTENSION*

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THE mechanism by which certain operative procedures on the sympathetic nervous system produce clinical improvement in well-selected cases of essential hypertension is unknown. There are numerous theoretical possibilities which have been ably reviewed by Heinbecker¹ and Coreoran and Page.² One obvious explanation is based upon Smith's contention³ that all cases of essential hypertension exhibit renal ischemia due to predominant constriction of the efferent glomerular arteriole; that is, that abolition of sympathetic impulses to the splanchnic region induces arteriolar relaxation and consequent increase in renal blood flow. If this is the correct explanation, the changes in the circulation pattern of the kidneys should be detectable by means of diodrast and inulin clearance studies. Alving, Adams, Grimson, Scott, and Sandiford,⁴ Coreoran and Page,² and Selzer and Friedman⁵ have reported no significant renal blood flow changes after operation in a few cases. It seems worth while to record our findings in five cases.

Our method of obtaining plasma clearances of diodrast and inulin as well as diodrast-Tm is being reported elsewhere;⁵ it is essentially that devised by Smith.⁶ Four of our patients were middle-aged women. Three of them, as well as the one male subject, aged 50 years, experienced entirely satisfactory symptomatic improvement, although in none was the mean blood pressure significantly reduced. One of the women received the supradiaphragmatic splanchnic section popularized by Peet on the other four patients the two-stage subdiaphragmatic operation advocated by Craig and Adson was performed. The one woman with a poor result belonged to this latter group. Preoperative clearance studies were done only after a prolonged period of hospital observation, when it was thought that the blood pressure had fallen as far as bed rest alone would permit. The studies were repeated at least ten days after operation when the patients were again comfortable and about to be allowed out of bed. In two instances a third set of observations was obtained about three months later. Unfortunately, diodrast-Tm was not determined preoperatively in two instances.

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3. Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W.: Effective Renal Blood Flow in Subjects With Essential Hypertension, *J. Clin. Investigation* 20: 637, 1941.
4. Alving, A. S., Adams, W., Grimson, K. S., Scott, C., and Sandiford, I.: The Effect of Bilateral Sympathectomy on the Cardiorenal System in Essential Hypertension, *Proc. Central Soc. Clin. Research* 13: 39, 1940.
5. Findley, T., Edwards, J. C., Clinton, E., and White, H. L.: Diodrast, Phenol Red, and Inulin Clearances in Hypertension and Nephritis. Submitted for publication.
6. Smith, H. W., Goldring, W., and Chasis, H.: The Measurement of the Tubular Excretory Mass, Effective Renal Blood Flow and Filtration Rate in the Normal Human Kidney, *J. Clin. Investigation* 17: 555, 1938.
7. Smith, H. W.: Note on the Methods in the Diseased Kidney, *J. Clin. Investigation* 20: 631, 1941.
8. Selzer, A., and Friedman, M.: Effect of Bilateral Splanchnicectomy Upon Renal Blood Flow in Hypertension, *Proc. Soc. Exper. Biol. & Med.* 48: 429, 1941.

and D-Tm fell progressively. To our knowledge, this phenomenon has not been described. It appears to represent progressive tubular degeneration.

Of the other three subjects there is little to be said except that no significant change in renal function occurred. It seems unlikely that inclusion of preoperative D-Tm in subjects A. G. and H. B. would have given cause to modify this statement.

DISCUSSION

We have elsewhere stated⁵ that a high $\frac{IC}{DC}$ ratio is in itself incapable of demonstrating efferent glomerular arteriolar spasm because it can also be accounted for by diminished tubular extraction of diodrast. Smith⁷ believes that renal ischemia is characterized by a low $\frac{DC}{D-Tm}$ ratio, and we have supported this contention. Subject P. C., however, shows how even this ratio may be altered by unexpected variations in tubular function, and adds one more complicating factor to the interpretation of clearances when no renal vein blood is available for renal extraction study. Diminished diodrast extraction may so alter DC and D-Tm values as to obscure coexisting renal ischemia.

There is nothing in this limited experience which leads us to believe that the circulation pattern of the human hypertensive kidney was appreciably altered by the surgical procedures employed. It might be argued that such an effect could be demonstrated only early in the disease before organic vascular changes take place, but it was precisely in this type of uncomplicated hypertension that we were unable to demonstrate consistent renal ischemia even by the $\frac{DC}{D-Tm}$ ratio.⁵ It might also be argued that since none of these operations produced significant drops in blood pressure, no change in renal hemodynamics should have been expected. Having as yet no pertinent data, we are unable to answer this objection, but we believe that the changes in blood pressure which occasionally follow surgical attacks on the sympathetic nervous system are nonspecific in nature and not fundamentally related to the cause of the disease.

CONCLUSION

In five cases of essential hypertension, sympathectomy produced no important changes in renal blood flow.

REFERENCES

1. Heinbecker, P.: A Role for Surgeons in the Problem of Essential Hypertension, *Ann. Surg.* 122: 1101, 1940.
2. Corcoran, A. C., and Page, I. H.: Renal Blood Flow and Sympathectomy in Hypertension, *Arch. Surg.* 42: 1072, 1941.

from the ribs along with the periosteum and still attached to it; (4) in case of deep infection only the skin and fascia of the incision need be reopened to drain the infected space adequately at its dependent point, thus insuring a more comfortable and shorter convalescence; (5) a fresh clean operative area for a lower thoracoplasty is maintained posteriorly; (6) a better cosmetic result is obtained; and (7) less bleeding and shock occur, making the procedure particularly useful in patients with poor reserve. Furthermore, if it becomes advisable to interrupt the operation because of unfavorable change in the patient's condition, the incision can be closed much more rapidly than can a posterior wound. We had hoped, also, that because of noninterference with the superficial back muscles there might be less tendency to scoliosis, but this has not proved to be the case. This incision is particularly desirable for patients with an empyema already drained posteriorly, as it enables one to remove the upper ribs and the anterolateral portions of the lower in a clean area away from the drainage opening.



Fig. 1.—A, Axillary incision first stage; B, posterior incision second stage; C, anterior view of patient following completed thoracoplasty.

In employing this incision, instruments somewhat longer than is customary are highly desirable. Naturally, the exposure is not as wide as with the usual posterior approach, yet no undue difficulty should be experienced. Retracting is easy with abdominal and flat malleable retractors posteriorly and superiorly. Once the periosteum, the anterior scalene attachment, and the vessels are pushed away from the first rib, they and the lower trunks of the brachial plexus are readily held away from the rib with a long flat retractor while the posterior portion is cleaned to the tubercle or transverse process. The one disadvantage we have found has been that occasionally a true neuritis develops in the corresponding arm with even temporary weakness in the hand. We have

THORACOPLASTY THROUGH SHORT LATERAL AND POSTERIOR INCISIONS

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FOR some years we have tried to modify the usual incision for paravertebral thoracoplasty so as to cause less damage to muscles, with consequent opening of tissue planes, and to achieve a better cosmetic result. This last is of considerable importance in women, provided that the essential parts of the operative procedure can be properly performed with adequate rib removal and without undue trauma to tissues and the underlying lung.

First, we tried starting the usual posterior incision not higher than the level of the spine of the scapula, as first advocated by Roux, of Lausanne. This gives adequate exposure and saves the upper part of the trapezius and a small portion of the rhomboids. However, all the planes of the back have been opened, so that should a deep infection occur (fortunately a rare but most dreaded accident), the result is usually a complete dehiscence of the incision and a large, gaping, deep, grossly infected wound which at best will require a long, slow period of healing, often with resulting marked disfigurement. We next became interested in the multiple incision procedure proposed by Wangenstein and the muscle-splitting operation advocated by Head, but felt these were not entirely satisfactory. Hudson's transverse incision along the third rib anteriorly finally gave us the clue to what in our hands seems to be the solution to our problem. His incision, while perfectly suitable for men, is unsightly in women; nevertheless, it has demonstrated that the upper stage of a paravertebral thoracoplasty can be performed through some sort of anterior or lateral incision without any damage to the back muscles whatsoever. After working with Hudson's transverse anterior incision, a vertical anterolateral incision along the lateral border of the pectoralis major, and a vertical incision in the midaxilla, it becomes obvious that this last incision fulfills all the requirements: (1) Adequate exposure is obtained permitting the removal of the upper three or four ribs from the sternum to their necks if desired, either with or without the transverse processes; (2) the muscles and tissue planes of the back are not disturbed in any way; (3) no muscles are cut except the pectoralis minor, which may or may not be severed at its coracoid attachment, the insertions of the serratus magnus being stripped away

attributed this to the rather prolonged stretching of the brachial plexus due to the position of the arm, and also to the pressure of the retractors. This has always cleared, however. Also, even with our long instruments we have felt the procedure to be less practical for excessively fat women or the occasional large, heavily muscled male.

The second and third stages of the thoracoplasty may readily be performed through a short incision around the angle of the scapula exposing the undefended intermuscular space between the trapezius and the latissimus dorsi muscles, the so-called auscultatory triangle. With the scapula in its relaxed position and after mobilizing the borders of the trapezius, the rhomboids, and the latissimus, the ribs may be readily removed from the third to the ninth or tenth. With scapula and muscles thus mobilized, the scapula is retracted about with great ease to expose any part of the operative field desired.

Both of these incisions are not new and have been in use in South America for some time. The Finochietto's have proposed these procedures and have extensively developed and advocated their use. Dr. Aguilar, also, is most enthusiastic about this method, and employs it routinely using local anesthesia throughout. His monograph on *Extrapleural Thoracoplasty* explains in great detail the development of the various incisions. We intend to present here only our experiences with them, with certain minor modifications.

PROCEDURE

Proper position of the patient is of the utmost importance. The patient is placed directly on his good side and the arm of the operated side elevated to an angle of about 120° with the trunk. The elbow is flexed to 90° , and the whole arm then carried forward across the body in order to relax the pectoralis major. To maintain this position, the forearm may be either bandaged or taped to the transverse bar of the ordinary ether screen frame. As is shown in the illustration, we have devised a much heavier frame constructed of strip metal. This fits into the lugs on the runners at the side of the operating table, and may be elevated or lowered as well as pushed forward or back. Since it is quite rigid, we have found it to be particularly serviceable whenever we have needed a support for the arm, as in this operation. In addition, the swiveled horizontal rods on either side of the transverse bar afford, when draped, a larger protected sterile field for the surgeon and his assistants.

After the skin has been prepared and the patient draped, a straight incision is made in the midaxilla between the pectoralis major and the latissimus dorsi. This begins at the lower border of the axillary hair and extends to the fifth rib, a distance of about five inches. The incision is carried through the axillary fat pad and the pectoralis major, identified and freed so that it may be lifted away from the chest. It is some-

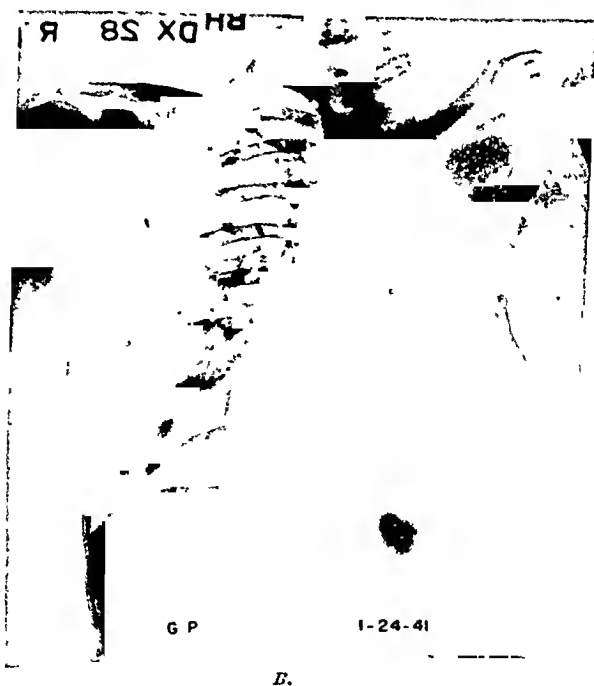
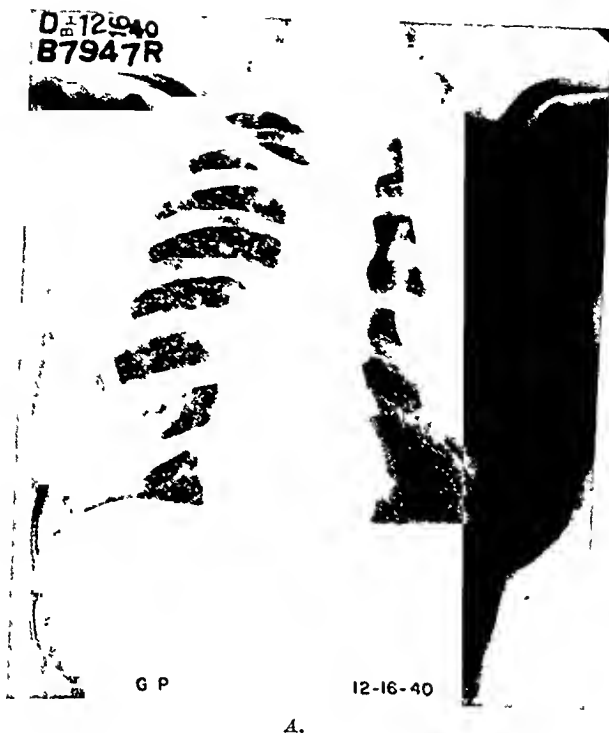


Fig. 2.—A, X-ray following first stage axillary incision; B, x-ray following completion of thoracoplasty by posterior stage.

concave spatula and the rib freed to its neck and disarticulated. The third rib is treated in like manner, and then the fourth if that also is to be removed. Ordinarily, except in cases of empyema, we advise the removal of only three ribs. Exceptions may be made, however, when it is felt that a four rib thoracoplasty is all that is required, or if there is no undue paradoxical respiration, the condition of the patient is excellent, and the type of lesion permits. After removal of the ribs, all that is necessary is to close the deep layer of the superficial fascia and skin, which we do with interrupted black silk sutures. There is very little bleeding throughout, little or no shock from the procedure, and so far in our experience a considerably more comfortable postoperative convalescence. The operation itself, however, is not a short cut, but takes time and patience with particular attention to position, exposure, relaxation, and adequate but gentle retraction. If the incision is carried too high into the axilla itself, a slight bowstring tendency may persist in the scar.

After the usual interval of about three weeks, the second stage is performed. As in the first stage, the patient is placed in the lateral position but with his uppermost arm at his side so as to relax the latissimus dorsi and thus the scapula. A short-curved incision about six inches long is made about the angle of the scapula to expose the intermuscular space. The presenting borders of the trapezius, rhomboids, and latissimus are picked up and the fascia dissected so as to mobilize them thoroughly. This provides perfect mobility of the scapula, which should be in its relaxed normal position at the start. With retractors under the scapula, and muscles, good exposure in any direction may be obtained, so that the desired number of ribs with or without transverse processes may be readily removed to as far forward as the midaxillary or anterior axillary line. Here again no muscles are divided, bleeding is minimal, and closure is attained by suture of only the superficial fascia and skin.

INSTRUMENTS

In order to facilitate removal of the ribs in both of the procedures just described, we have devised four instruments.* One of these is a slight modification of a periosteal raspator† and elevator‡ made some years ago for Dr. A. V. S. Lambert and one of us and consists of an Alexander type raspator and a Doyen type curved elevator. For our present purposes we have lengthened the shaft of the raspator end. This has not interfered with, and has actually enhanced the usefulness of the instrument for all other work on the thoracic cage. It is very strong and light, combines two instruments in one, and, due to its cylindrical body, fits comfortably into the hand without slipping or causing fatigue.

*With the kind cooperation of the Kny-Scherer Corporation.

†Made by Tiemann and Company.

times a good plan also to identify the pectoralis minor and divide it at its insertion into the coracoid, as this gives added relaxation and space as well as direct exposure of the thoracic cage. Next the long thoracic nerve is picked up and retracted, and the periosteum of the third or even the fourth rib incised through the fibers of the serratus from as far forward as desired to the posterior axillary line. This portion of the rib is stripped of periosteum and removed. The second rib is similarly treated except that it is divided somewhat farther back. The periosteum of the first rib, which is now found to be well exposed, is incised along the lower border from the cartilage to as far back as possible. With a protective finger along the upper edge of the rib, the periosteum is then stripped from the superior and inferior surfaces, and the attachment of the scalenus anticus separated with the long elevator. The vessels and



Fig. 3.—Anesthesia screen used for arm support showing movable wings.

brachial plexus are now gently retracted upward as the posterior portion of the rib is cleared. As the long ribbon retractor well protects these structures, the rib may be divided at or close to its tubercle with long rib shears and the remainder removed with a nine-inch Horsley rongeur. Once the first rib is removed the traction on the arm may be relaxed. The posterior ends of the second, third, and fourth ribs are now readily accessible. Starting with the second, the periosteum and muscles may be stripped back to and including the transverse process, and the rib and process removed with long rib shears and rongeurs. Instead, if preferred, the costovertebral joint may be entered with the long

concave spatula and the rib freed to its neck and disarticulated. The third rib is treated in like manner, and then the fourth if that also is to be removed. Ordinarily, except in cases of empyema, we advise the removal of only three ribs. Exceptions may be made, however, when it is felt that a four rib thoracoplasty is all that is required, or if there is no undue paradoxical respiration, the condition of the patient is excellent, and the type of lesion permits. After removal of the ribs, all that is necessary is to close the deep layer of the superficial fascia and skin, which we do with interrupted black silk sutures. There is very little bleeding throughout, little or no shock from the procedure, and so far in our experience a considerably more comfortable postoperative convalescence. The operation itself, however, is not a short cut, but takes time and patience with particular attention to position, exposure, relaxation, and adequate but gentle retraction. If the incision is carried too high into the axilla itself, a slight bowstring tendency may persist in the scar.

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The other three instruments were made particularly for this type of work. They form a set and are identical in weight and design. Each is ten inches in length and has a good-sized ovoid handle with several plane surfaces. This again permits of a comfortable grasp without slipping or cramping.

1. The shaft of the first is slightly decurved and ends in a raspatory of the Alexander type.

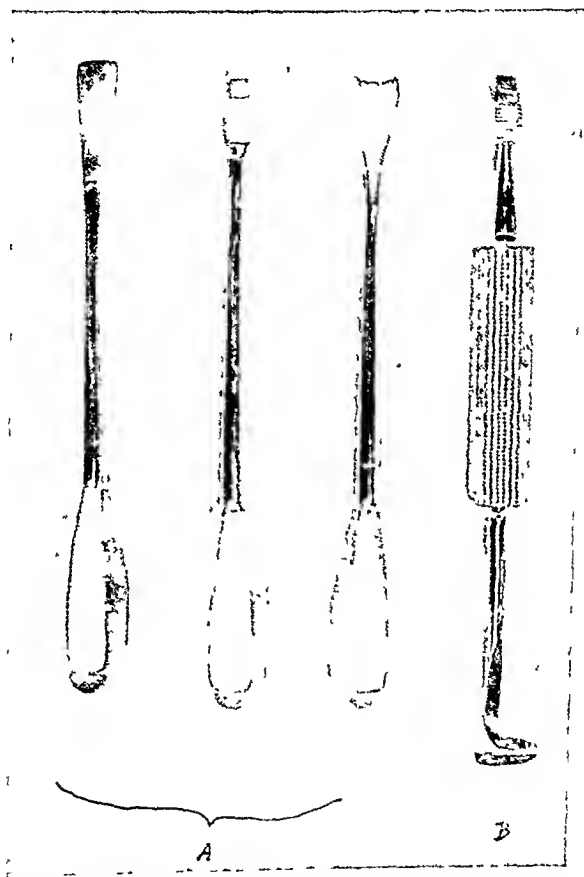


Fig. 4.—Special instruments described and advocated. A, Set of long shank elevators and raspatory. B, revised Berry-Lambert raspatory.

2. In the second instrument, the head consists of a slightly concave spatula, the center of which has a sharp cutting edge guarded on either side by the blunt slightly protruding margins of the head. 3. The head of the third is slightly concave and square with a straight drill edge and rounded dull corners. Although these instruments are not as long as those used by R. Finochietto and Aguilar, we have found them adequate. For cutting the ribs and transverse processes any of the long rib shears and rongeurs may be employed.

SUMMARY AND CONCLUSIONS

Two variations of the commonly used posterior hockey-stick incision for paravertebral thoracoplasty are described.

We believe these techniques to be the methods of choice in many instances because:

1. Both provide adequate exposure and permit thoroughness and safety of operation just as with the long posterior incision.
2. Neither one divides muscle, thus preserving the muscle and fascial planes of the back.
3. Only skin and fascia need be opened for drainage of a deep wound infection, which is usually localized by the barrier of the undisturbed muscles and fascial planes, thus avoiding the necessity of a wide gaping wound in the back.
4. By using the lateral incision for the first stage a fresh operative area is preserved posteriorly for the second stage.
5. Bleeding and shock are lessened in both procedures.
6. Convalescence is apparently more comfortable.
7. Better cosmetic results are obtained, an important consideration in women.

A disadvantage is the occasional temporary neuritis with weakness of forearm and hand that may develop after the first stage. This is probably due to stretching or retraction of the brachial plexus.

Special long instruments are described. These are not absolutely necessary, but instruments of equal or increased length greatly facilitate the procedure.

We wish to emphasize that similar operative techniques have been described and are being employed by Finochietto, Aguilar, and their associates. Their work undoubtedly preceded ours, but having arrived at the same conclusions quite independently, we believe it worth while to describe these modifications and along with them to urge their adoption in suitable instances.

REFERENCES

1. Aguilar, H.: *La Toracoplastia en el tratamiento de la tuberculosis pulmonar*, Buenos Aires, 1938, El Ateneo.
2. Finochietto, E.: *La Toracoplastia alta por medio de la incisión paradójica*, Prensa méd. argent. 22: 1797, 1935.
3. Finochietto, R.: *Toracoplastia, La incisión paradójica de Enrique Finochietto*, Detalles de técnica, Prensa méd. argent. 23: 789, 1936.
4. Finochietto, R.: *Thoracoplasty Without Section of Muscles*, J. Thoracic Surg. 9: 450, 1940.
5. Head, J. R.: *Extrapleural Thoracoplasty: A Muscle Splitting Operation*, Arch. Surg. 16: 1075, 1928.
6. Head, J. R.: *Extrapleural Thoracoplasty; Further Experiences With a Muscle Splitting Operation*, J. Thoracic Surg. 8: 55, 1938.
7. Hudson, W. A.: *A Selective Type of Thoracoplasty Operation*, J. Thoracic Surg. 9: 357, 1940.
8. Waugensteen, O. H.: *Thoracoplasty for Tuberculosis and Chronic Empyema Through Short Incisions*, J. Thoracic Surg. 8: 60, 1938.

SHOCK IN CONTROL AND SPLENECTOMIZED ANIMALS UNDER ETHER AND PENTOBARBITAL SODIUM ANESTHESIA

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IT HAS been demonstrated by the work of Seeley, Essex, and Mann that sodium amytal (sodium iso-amylethyl barbiturate) alone or preliminary to ether anesthesia results in a marked delay in the onset of shock produced by intestinal manipulation as compared to results with ether anesthesia alone. Shock was considered to be present when the systolic blood pressure decreased to 70 mm. of mercury. With ether anesthesia alone shock occurred on an average of three hours and fifty-three minutes from the beginning of intestinal manipulation, while with sodium amytal alone shock did not appear on the average until eleven hours and thirty-three minutes from the time intestinal manipulation was begun. One of us (Kendrick) obtained strikingly similar results with ether and pentobarbital sodium using the methods described by Seeley, Essex, and Mann. Because of the possibility of a practical application of these findings to the care of patients injured in war or in accidents, further work on this problem seemed advisable.

As a result of a series of researches in this laboratory (Searles and Essex; Essex, Seeley, Higgins, and Mann; and Hausner, Essex, and Mann) it has also been demonstrated that anesthesia with certain barbiturates causes hemodilution for which the spleen is largely responsible since this organ under the influence of barbiturates removes from currency a large volume of erythrocytes. We wished to ascertain whether the spleen plays a role in the delay in the onset of shock when barbiturates are used. It may logically be asked whether the barbiturates would be of value in delaying the onset of traumatic shock induced under ether anesthesia if given to control and splenectomized dogs when shock was considered imminent. If so, when would be the optimal time to give the drug and how long after intestinal trauma might it be expected to produce effective results? The work described in this paper was done in the hope of answering these questions.

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Work done at the Institute of Experimental Medicine.

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METHODS

All experiments were done on dogs using ether and pentobarbital sodium anesthesia. Shock was produced by delivering the small intestine outside of the abdominal cavity and gently massaging it throughout its entire length for thirty to forty minutes, after which it remained exposed on the anterior abdominal wall. The blood pressure in the femoral artery was recorded on a standard kymograph. As in previous experiments in this laboratory the animals were considered to be in a state of shock when the systolic blood pressure had declined to 70 mm. of mercury. It was recognized that the arterial blood pressure might not accurately reflect the physiologic state of the animal. For that reason the blood pressure was not used as the criterion for the proper time to administer pentobarbital sodium. For this purpose the degree of hemoconcentration as determined by a Cenco-Sheard-Sanford photometer was considered more satisfactory. It had been found in the studies to which reference has already been made that the animals were in shock as indicated by the blood pressure when the average concentration of hemoglobin was 130 to 135 per cent, the preanesthetic concentration being arbitrarily called 100 per cent. Thus when the hemoconcentration had reached 130 to 135 per cent shock was considered imminent even though the blood pressure was being maintained near the control level.

The animals were anesthetized initially with ether, and narcosis was maintained by autoinhalation.² After the desired hemoconcentration had been attained ether anesthesia was discontinued and pentobarbital sodium was given intravenously in doses of 10 to 15 mg. per kilogram. In three experiments pentobarbital sodium was given when the hemoconcentration had reached 120 per cent, while in four experiments the hemoglobin was allowed to concentrate as much as 135 to 140 per cent before pentobarbital sodium was injected. To avoid a marked depression of blood pressure the drug was given very slowly in all experiments. In the series of seven experiments on splenectomized animals the spleen was removed immediately preceding intestinal manipulation.

RESULTS, SPLEEN PRESENT

In the four experiments in which the hemoglobin was allowed to concentrate 135 to 140 per cent, it required an average of twelve hours and thirty-five minutes to reduce the systolic blood pressure to 70 mm. of mercury. The average time required for the hemoconcentration to reach 130 to 140 per cent was three hours and eleven minutes. The average time that elapsed from the beginning of intestinal manipulation until the administration of pentobarbital sodium (15 mg. per kilogram) was three hours and fifty minutes. In the three experiments in which pentobarbital sodium was given when the hemoglobin had concentrated

to only 120 per cent, the systolic blood pressure did not decrease to 70 mm. of mercury until thirteen hours and twenty minutes after intestinal manipulation was begun. The greater the percentage of hemoglobin concentration at the time pentobarbital sodium was given the more rapidly shock occurred.

Rapid concentration of the blood always occurred while the animals were under ether anesthesia. When the administration of ether was discontinued and after pentobarbital sodium was given, a decrease in hemoglobin invariably occurred but hemoconcentration slowly developed as the experiments were continued (Fig. 1).

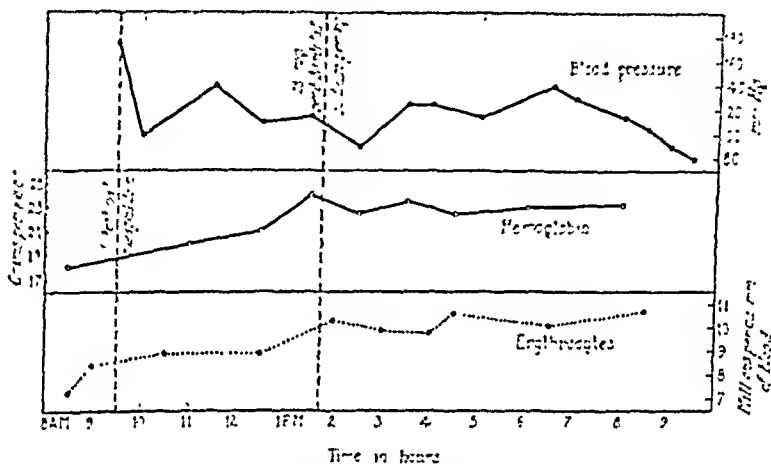


Fig. 1.—The effect of ether anesthesia, intestinal manipulation, and an injection of pentobarbital sodium on the blood pressure, hemoglobin concentration, and the number of erythrocytes in a dog with the spleen present.

RESULTS, SPLEEN ABSENT

In five experiments on splenectomized animals pentobarbital sodium in doses of 15 mg. per kilogram of body weight was injected intravenously after the hemoglobin had concentrated 135 to 140 per cent. The average time required for the systolic blood pressure to decline to 70 mm. of mercury was eight hours. During ether anesthesia the hemoconcentration was rapid. Following the injection of pentobarbital sodium the hemoconcentration increased, but much more slowly. The decrease in hemoglobin observed in experiments in which the spleen was present was not seen in the present series (Fig. 2).

In order to determine the effectiveness of smaller doses of pentobarbital sodium two experiments were done in which 10 mg. of the drug per kilogram of body weight were given after the hemoglobin had concentrated 130 to 140 per cent. In one experiment the blood pressure declined to shock level in eleven hours and forty-five minutes and in the other experiment shock occurred eleven hours and thirty minutes after intestinal manipulation.

COMMENT

The results of the experiments just reported indicate that doses of pentobarbital sodium as small as 10 mg. per kilogram of body weight were effective in delaying the decline of the blood pressure to a shock level even though intestinal manipulation and ether anesthesia had caused a concentration of hemoglobin that indicated that shock was impending.

That the spleen is an important factor in causing an apparent hemodilution following the injection of pentobarbital sodium has again been demonstrated by experiments on splenectomized animals in which hemodilution was not observed. The fact that the blood pressure was more rapidly reduced to a shock level in the splenectomized than in the non-splenectomized dogs would seem to indicate that the spleen is of considerable aid to the organism in its resistance to shock. The reservoir function of the spleen was probably its chief contribution. In the absence of the spleen the injection of pentobarbital sodium caused delay in the decline of blood pressure to a shock level as compared to results with ether anesthesia alone. The mechanism by which pentobarbital sodium is effective in this respect is not known. However, it should be emphasized that the animals in which the onset of shock was longest delayed were those that had received the smallest doses of pentobarbital sodium.

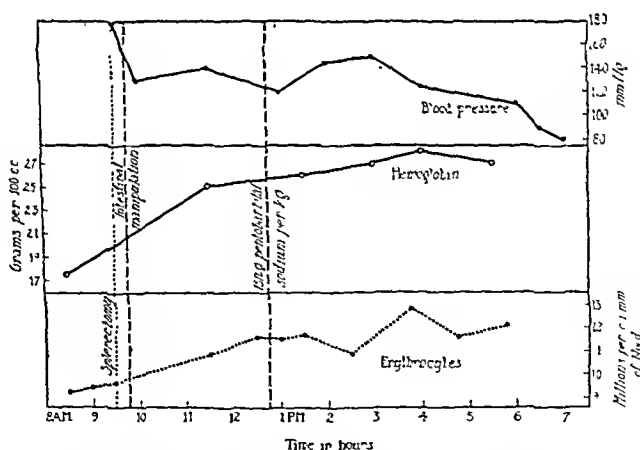


Fig. 2.—The effect of ether anesthesia, intestinal manipulation, and an injection of pentobarbital sodium on the blood pressure, the hemoglobin concentration, and the number of erythrocytes in a dog splenectomized just before the intestine was manipulated.

SUMMARY AND CONCLUSIONS

In this study an effort was made to determine the effectiveness of pentobarbital sodium in delaying shock when given after the hemoglobin had concentrated to a point at which shock might be considered

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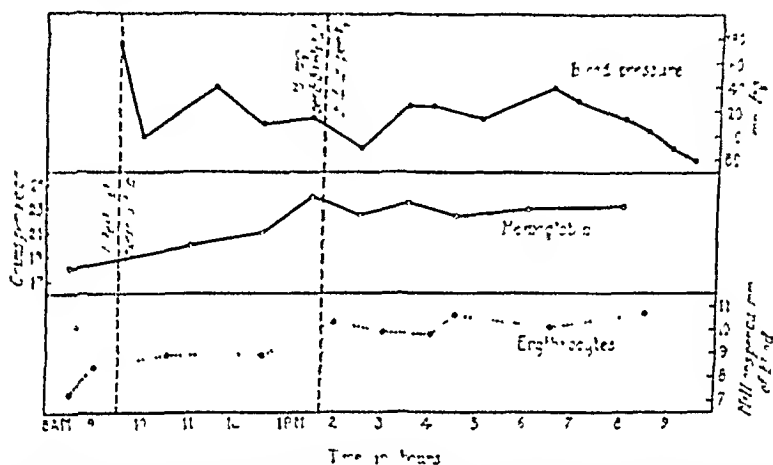


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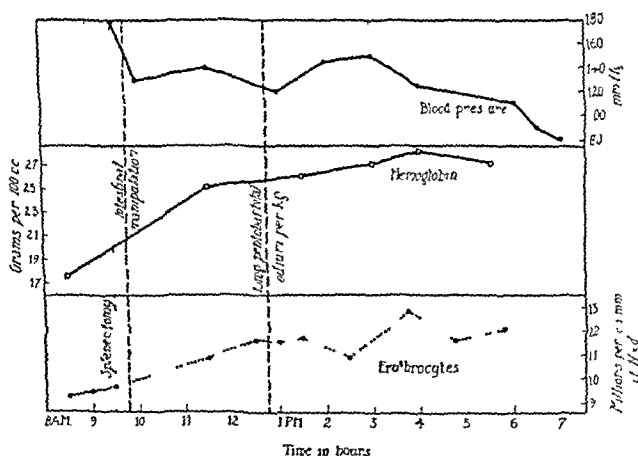


Fig. 2—The effect of ether anesthesia, intestinal manipulation, and an injection of pentobarbital sodium on the blood pressure, the hemoglobin concentration, and the number of erythrocytes in a dog splenectomized just before the intestine was manipulated.

SUMMARY AND CONCLUSIONS

In this study an effort was made to determine the effectiveness of pentobarbital sodium in delaying shock when given after the hemoglobin had concentrated to a point at which shock might be considered

imminent. The small intestine of dogs was manipulated under ether anesthesia. When the hemoconcentration had reached the desired level (120 to 140 per cent) pentobarbital sodium was given and ether anesthesia was discontinued. When the systolic blood pressure reached 70 mm. of mercury the animals were considered to be in a state of shock. A series of experiments was done on both nonsplenectomized and splenectomized dogs. In the former experiments a decrease in hemoglobin occurred immediately following the injection of the drug but this was followed by hemoconcentration which developed slowly. In the absence of the spleen hemodilution did not occur. In every experiment the greater the percentage of hemoglobin concentration the more rapidly shock developed. Under the conditions of our experiments the splenectomized animals went into shock more rapidly than the nonsplenectomized series of animals, which may be taken as an indication that the spleen is a definite aid to the organism in its resistance to shock. In all experiments, whether or not the spleen was present, shock developed more slowly than in previous experiments in which ether alone was used.

The evidence appears conclusive that shock develops more slowly in animals under pentobarbital sodium than in animals under ether anesthesia. The reason for this result is not known. These findings should not be taken to mean that the administration of pentobarbital sodium may be used as a prophylactic procedure in the treatment of the injured but rather that this drug is indicated as a supportive agent if the injured are to be given a general anesthetic such as ether.

REFERENCES

1. Essex, H. E., Seeley, S. F., Higgins, G. M., and Mann, F. C.: Effect of Ether Anesthesia and Amytal Anesthesia on the Erythrocytic Findings in Control and Splenectomized Dogs, *Proc. Soc. Exper. Biol. & Med.* 35: 154-156, 1936.
2. Hardenbergh, J. G., and Mann, F. C.: Auto-inhalation Method of Anesthesia in Canine Surgery, *J. Am. Vet. M. A.* 71: 493-501, 1927.
3. Hausner, Erich, Essex, H. E., and Mann, F. C.: Roentgenologic Observations on the Spleen of the Dog Under Ether, Sodium Amytal, Pentobarbital Sodium and Pentothal Sodium Anesthesia, *Am. J. Physiol.* 121: 387-391, 1938.
4. Kendrick, D. B., Jr.: Results of Intravenous and Intra-arterial Administration of Fluids in Traumatic Shock Produced Experimentally, *SURGERY* 6: 520-523, 1939.
5. Searles, P. W., and Essex, H. E.: Changes in Blood in the Course of Ether Anesthesia and Sodium Amytal Anesthesia, *Proc. Staff Meet., Mayo Clin.* 11: 481-482, 1936.
6. Seeley, S. F., Essex, H. E., and Mann, F. C.: Comparative Studies on Traumatic Shock Under Ether and Under Sodium Amytal Anesthesia; an Experimental Research, *Ann. Surg.* 104: 332-338, 1936.

SOME OBSERVATIONS ON THE RATE OF ABSORPTION FROM VARIOUS BODY TISSUES

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DURING the course of recent investigations concerning reactions to procaine in experimental animals, it appeared evident that the rate of absorption differed greatly according to the route of administration.¹ Since these experiments suggested that death ensued when the blood concentration of the drug reached a certain critical level, regardless of the site into which the toxic dose of procaine was injected, and since the circulating procaine is known to be rapidly destroyed or detoxified, it was felt that the wide differences in the lethal dose with different routes of administration were a reflection of different rates of absorption into the blood stream. These considerations led me to devise some simple experiments which might throw additional light upon this problem.

In all of the experiments except those dealing with the absorption of sulfanilamide, some indirect end point was selected rather than frequent and repeated chemical analysis of the blood which would have rendered the problem much more difficult. The general agreement of the experimental results obtained by using different effects of the various drugs which might reflect a therapeutic, toxic, or lethal blood concentration of the injected drug indicates that the method is valid. In all the experiments absorption from the subcutaneous, intramuscular, intrapleural, intraperitoneal, and intravenous routes of administration was studied. With each route control studies with distilled water given in the maximal amounts employed in the case of the drugs were carried out, and no symptoms and no deleterious effects were noted. Following intrapleural injections the animals were examined at autopsy and those whose lungs had been inadvertently damaged were excluded from consideration.

EXPERIMENTAL RESULTS

In all the experiments there seemed to be most rapid absorption from the intrapleural route. With some drugs, peritoneal absorption was apparently slower than that from subcutaneous or intramuscular tissues; with others it was more rapid.

Procaine.—In Table I are listed the results obtained from a large number of guinea-pigs given varying amounts of procaine hydrochloride by different routes. The median lethal dose varied from 41 mg. per

TABLE I

SHOWING VARIATION IN MEDIAN LETHAL DOSE OF PROCAINE IN GUINEA-PIGS ACCORDING TO THE ROUTE OF ADMINISTRATION

ROUTE OF ADMINISTRATION	MEDIAN LETHAL DOSE IN MG. PER KG.	NUMBER OF ANIMALS USED
Intravenous	41	54
Intrapleural	42	25
Thoracic paravertebral	115	10
Lumbar paravertebral	250	30
Intramuscular	320	25
Subcutaneous	410	56
Intraperitoneal	750	28

TABLE II

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF STRYCHNINE INTO GUINEA-PIGS BEFORE ONSET OF CONVULSIONS, LETHAL EFFECT OF VARYING DOSES ACCORDING TO ROUTE OF ADMINISTRATION

DOSE IN MG. PER KG.	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- MUSCULAR	SUB- CUTANEOUS	INTRA- PERITONEAL
0.16	No			No	
0.48	7	No		No	
0.64		8		No	No
1.6	5 D	20(2) D	No	No	No
2.4	3.5(3) D	16(3) D	215(3) D*	No(3)	No(3)
3.84	2.5 D	11 D	140 D	510 D	No
5.76	1.5 D	15 D	132 D	360 D	No
9.6		6 D	118 D	340 D	420 D

Absence of convulsions is indicated by "No."

When more than one animal was used, the number is put in parentheses.

"D" indicates that death occurred.

(These designations are also used in Tables V, VI, VII, VIII, and IX.)

*Two of the three animals died.

TABLE III

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF STRYCHNINE INTO MICE BEFORE ONSET OF CONVULSIONS, LETHAL EFFECT OF VARYING DOSES ACCORDING TO ROUTE OF ADMINISTRATION

DOSE IN MG. PER ANIMAL	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- MUSCULAR	SUB- CUTANEOUS	INTRA- PERITONEAL
0.02	5 (5) D	25(7) D	No	No	No
0.04	1.7(3) D	23(3) D	250(3) D	370(3) D*	D†

*Two of the three animals died.

†Only one of the four animals had convulsions and only one died.

The mice weighed between 25 and 30 Gm.

TABLE IV

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF MORPHINE SULFATE INTO MICE BEFORE ONSET OF SLEEP AND BEFORE DEATH

DOSE IN MG. PER ANIMAL	ROUTE OF ADMINISTRATION									
	INTRA- VENOUS		INTRA- PLEURAL		INTRA- MUSCULAR		SUB- CUTANEOUS		INTRA- PERITONEAL	
	SLEEP	DEATH	SLEEP	DEATH	SLEEP	DEATH	SLEEP	DEATH	SLEEP	DEATH
155*	30(2)	80(2)	320(2)	450(2)	No	No	2400	2700	No	No
167†	1	25	297(3)	465(3)	600	3900	4200	4400	1100	No

*Also 4 mg. atropine.

†Also 4.5 mg. atropine.

kilogram with intravenous injections to 750 with intraperitoneal injections. The median lethal dose was very small with intravenous and intrapleural injections and was progressively larger when the drug was given in the thoracic paravertebral space, lumbar paravertebral space, intramuscular tissues, subcutaneous tissues, and the peritoneal cavity. Apparently the rapidity of absorption of the drug varied in this order.

Strychnine.—Strychnine was administered in different doses and by various routes to guinea-pigs and to mice. The results are recorded in Tables II and III. The interval after injection of the drug before the onset of convulsions was shortest when the drug was given intravenously. It was brief following intrapleural injections, somewhat longer after intramuscular injections, still longer after subcutaneous injections, and longest after intraperitoneal injections. Also, it will be noted that the rapidity or the delay in onset of convulsions varied directly with the size of the lethal dose. One would judge that the rate of absorption of the drug is most rapid from the pleura, somewhat slower from the muscles, still slower from the subcutaneous tissues, and slowest from the peritoneum.

Morphine.—The same conclusions are reached from study of the interval following injection of morphine into mice before onset of sleep and of death (Table IV).

Phenolsulfonphthalein.—At intervals of a week a normal, healthy mongrel dog was given 1 c.c. of phenolsulfonphthalein by various routes following introduction of a catheter into the bladder. The appearance time of the drug in the urine was noted, total specimens were collected at fifteen-minute intervals, and the excretion curve was plotted. An intravenous injection was carried out at the beginning and at the end of the experiment. The agreement in these excretion curves was evidence that no essential change in kidney function had occurred. The intravenous excretion curve in Fig. 1 is an average of the two. If the rapidity of excretion is a rough measure of the rapidity of absorption, one would conclude that absorption is most rapid from the pleura, less rapid from the subcutaneous tissues, and slowest from the peritoneum.

Metrazol.—Different amounts of metrazol were administered by various routes to guinea-pigs and to mice, and the interval after injection before onset of convulsions was recorded (Tables V and VI). Judging by these observations and by the lethal dose with the different routes, one would assume that the drug is absorbed most rapidly from the pleura, less rapidly from the peritoneum, still more slowly from the muscles, and most slowly from the subcutaneous tissues.

Coramine.—Similar experiments were carried out with coramine (Tables VII and VIII) and similar results were obtained.

Nembutal.—A number of mice were given 2.5 mg. of nembutal by several routes, and the interval before sleep was noted. The onset of sleep was almost instantaneous after intravenous injections, was very

TABLE V

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF METEAZOL INTO GUINEA-PIGS BEFORE ONSET OF CONVULSIONS. LETHAL EFFECT OF VARYING DOSES ACCORDING TO ROUTE OF ADMINISTRATION

DOSE IN MG. PER KG.	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- PERITONEAL	INTRA- MUSCULAR	SUB- CUTANEOUS
0.2	4				
0.3	4 D	11	No	No	No
0.4	4 D	11 D	180	230 D	720
0.6	1.5 D	6.5(2) D	120	540	1500
1.0	1.5(2) D	9 D	100 D	100 D	600 D

TABLE VI

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF METEAZOL INTO MICE BEFORE ONSET OF CONVULSIONS

DOSE IN MG. PER ANIMAL	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- PERITONEAL	INTRA- MUSCULAR	SUB- CUTANEOUS
3.33	1.7 (4)	4 (5)	90 (6)	162 (5)	167 (5)

All the animals died.

The mice weighed between 25 and 30 Gm.

TABLE VII

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF CORAMINE INTO GUINEA-PIGS BEFORE ONSET OF CONVULSIONS. LETHAL EFFECT OF VARYING DOSES ACCORDING TO ROUTE OF ADMINISTRATION

DOSE IN MG. PER KG.	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- PERITONEAL	INTRA- MUSCULAR	SUB- CUTANEOUS
1.25	7 D	20(2) D*	143(2)	No	No
2.5	4 D	21(3) D	180 D	900 D	1260 D
3.75	4 D	21 D	60 D	360 D	330 D

*One of the two animals died.

TABLE VIII

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF CORAMINE INTO MICE BEFORE ONSET OF CONVULSIONS

DOSE IN MG. PER ANIMAL	ROUTE OF ADMINISTRATION				
	INTRA- VENOUS	INTRA- PLEURAL	INTRA- PERITONEAL	INTRA- MUSCULAR	SUB- CUTANEOUS
25	2 (3)	4 (3)	100 (3)	350 (2)	310 (2)

All the animals died.

The mice weighed between 25 and 30 Gm.

TABLE IX

TIME ELAPSING (IN SECONDS) AFTER INJECTION OF NEMBUTAL INTO MICE BEFORE ONSET OF SLEEP

ROUTE OF ADMINISTRATION				
INTRAVENOUS	INTRAPLEURAL	INTRAPERITONEAL	INTRAMUSCULAR	SUBCUTANEOUS
1 (4)	40 (5)	120 (5)	182 (5)	280 (4)

The mice weighed between 25 and 30 Gm.

Each animal was given 2.5 mg.

rapid after intrapleural injections, somewhat less rapid after intraperitoneal injections, still slower after intramuscular injections, and slowest after subcutaneous injections.

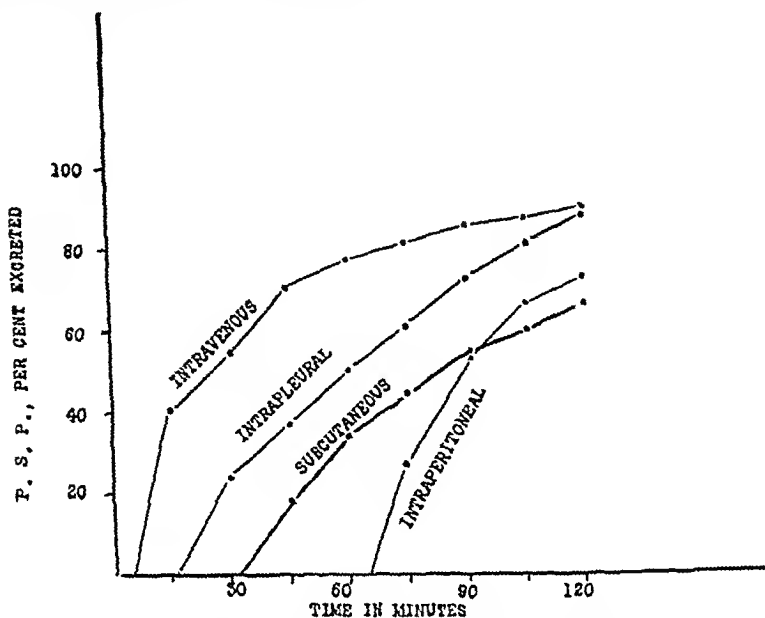


Fig. 1.—Excretion curves of phenolsulfonphthalein administered by various routes. The appearance time is indicated by the point at which the curve begins.

Sulfanilamide.—Three normal healthy mongrel dogs previously starved for twenty-four hours were anesthetized with ether and given 100 mg. of finely powdered sulfanilamide per kilogram of body weight. In one the powder was put into the left thoracic cavity through an intercostal incision. The lung was re-expanded and the wound closed. In a second dog the sulfanilamide was similarly introduced into the peritoneal cavity through a midline incision, and in the third it was placed in a large subcutaneous pocket made in the left upper quadrant of the abdomen. Specimens of blood were taken frequently for assay by the technique of Bratton and Marshall.² As recorded in Fig. 2, absorption was most rapid from the pleura and least rapid from the subcutaneous tissues. For example, in thirty-five minutes the concentration in the blood was 12.5 mg. per cent in the dog given the drug intrapleurally, 3.48 mg. per cent in the dog given the drug intraperitoneally, and 0.598 mg. per cent in the one given the drug subcutaneously.

Haag, Spealman, and McCue³ recently conducted some studies on the absorption of sulfanilamide in dogs and concluded that absorption is as good from the pleura and peritoneum as from the gastrointestinal tract. Although they did not do blood assays in the early period after administration of the drug as frequently as I did, their results also suggest that

absorption is actually more rapid from the pleura than from the peritoneum or the gastrointestinal tract.

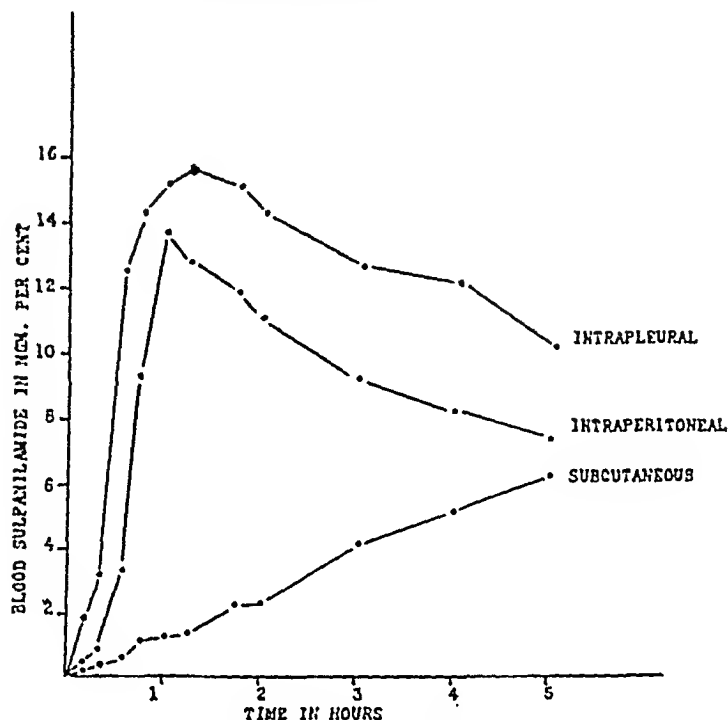


Fig. 2.—Absorption curves of sulfanilamide given by different routes.

DISCUSSION

The present study is by no means complete or exhaustive, and many questions arise. I have made no attempt to determine the relative roles of lymphatic and capillary absorption, the influence of depth and rapidity of respirations on the rate of absorption from pleura and peritoneum, and the question of the size of the molecule in determining whether peritoneal absorption is rapid or very slow. One wonders whether the slow absorption from the peritoneal cavity may result in part from absorption of some of the injected material into the portal circulation with retention or actual chemical change of the drug in the liver. I do not know what influence a local inflammatory process in the pleura or the peritoneum has upon the rate of absorption. These and other matters deserve further study. The experiments reported do demonstrate that with all the drugs studied there is apparently very great difference in the rapidity of absorption from various body tissues and serous cavities. They demonstrate further that with all the drugs studied and in all the species of animals employed, absorption from the pleura is very much more rapid than from any other tissue investigated.

With some drugs peritoneal absorption is relatively rapid, with others very slow.

These studies permit one to emphasize the importance of investigating adequately the rate of absorption of any drug from all the body tissues into which it might be purposefully or inadvertently introduced. This investigation is necessary in order to obtain the best therapeutic effect and to avoid toxic reactions. Such studies should lead to better clinical results and to fewer alarming and even fatal reactions.

REFERENCES

1. Shumacker, H. B., Jr.: Reactions to Local Anesthetic Agents. I. Experimental Studies With Procaine, *SURGERY* 10: 119-133, 1941.
2. Bratton, A. C., and Marshall, E. K., Jr.: A New Coupling Component for Sulfanilamide Determination, *J. Biol. Chem.* 128: 537-550, 1939.
3. Haag, H. B., Spealman, C. R., and McCue, H. M.: Comparative Absorption Rate of Sulfanilamide From the Pleural Cavity, Peritoneal Cavity, and Gastrointestinal Tract in Dogs, *SURGERY* 10: 572-575, 1941.

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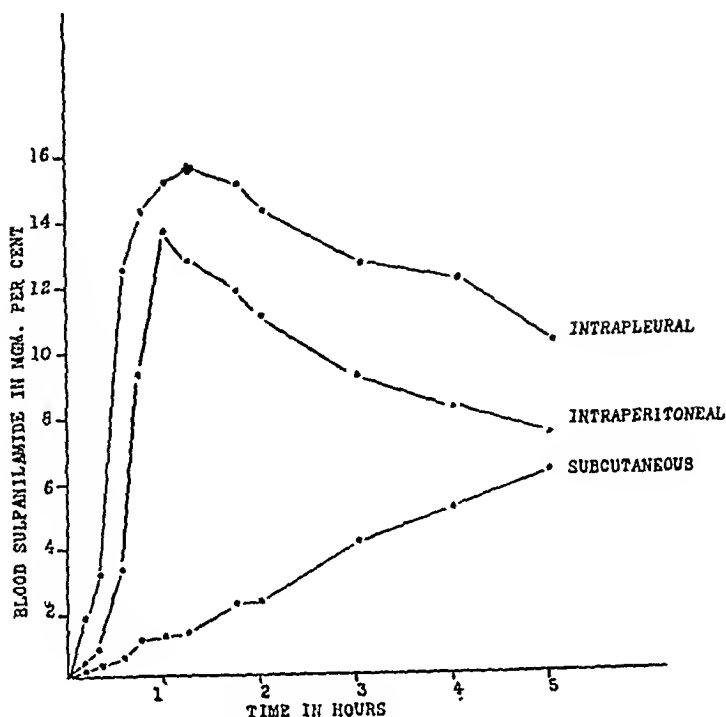


Fig. 2.—Absorption curves of sulfanilamide given by different routes.

DISCUSSION

The present study is by no means complete or exhaustive, and many questions arise. I have made no attempt to determine the relative roles of lymphatic and capillary absorption, the influence of depth and rapidity of respirations on the rate of absorption from pleura and peritoneum, and the question of the size of the molecule in determining whether peritoneal absorption is rapid or very slow. One wonders whether the slow absorption from the peritoneal cavity may result in part from absorption of some of the injected material into the portal circulation with retention or actual chemical change of the drug in the liver. I do not know what influence a local inflammatory process in the pleura or the peritoneum has upon the rate of absorption. These and other matters deserve further study. The experiments reported do demonstrate that with all the drugs studied there is apparently very great difference in the rapidity of absorption from various body tissues and serous cavities. They demonstrate further that with all the drugs studied and in all the species of animals employed, absorption from the pleura is very much more rapid than from any other tissue investigated.

In either case the procedure is the same as for repair of any other similar defect where the reconstruction is effected by a half-thickness skin graft. However, it can readily be seen that reconstruction is more difficult here because of the necessity of grafting over a rounded surface. Because of the potential variation in size encountered as a result of normal physiologic response, the problem of maintaining proper apposition of the graft is again exaggerated. These difficulties, however, can be overcome largely by procuring a half-thickness skin graft large enough to encase completely the entire circumference of the penis. External urethrotomy²² and suprapubic cystotomy have been suggested as preliminary procedures, but are unnecessary. Cases of complete traumatic avulsion of the skin of the penis and scrotum which were seen by a surgeon within the first few hours following the accident have been reported. In some of these repair was attempted after treating the patient for two or three days.^{15, 27} Grafting was not attempted in one case¹⁴ until ten days after the injury. Because of the excessive contamination to which a wound is subjected in this region, it is imperative to attempt to obtain primary healing in all cases. This is possible only if the surgeon sees the patient within the contaminated period and the patient's general condition permits an adequate débridement. A graft should then be applied immediately. If these precautions are taken, a full take of the graft with satisfactory healing by primary union may be expected. Following débridement, the graft is wrapped about the penis and attached either by interrupted or continuous sutures along the margins of the defect at or near the corona and toward the base of the penis. In order that firm fixation may be obtained, the graft then is attached to the shaft of the penis down the line where its two borders overlap. Either a grease or moist saline solution dressing of fine mesh gauze is applied directly to the surface of the graft and adjacent to this a few thicknesses of sterile dry gauze are placed. Over these a sea sponge or sterile waste pressure dressing is applied in order that adequate and uniformly distributed pressure may be maintained along the entire shaft of the penis. The pressure dressing is fixed with adhesive, which not only encircles the dressing over the shaft of the penis but extends from the shaft up to the pubis and over the abdomen, thus supporting the dressing.

Other methods of repairing surface defects of the penis have been suggested and used, such as scrotal flap,¹⁰ single pedicle skin transplant, and tube pedicle transplant. Whereas the writer has had no occasion to employ the latter two methods, on one occasion repair of a surface defect of the penis was attempted by means of a pedicle formed by dissecting a cuff of scrotal skin and attaching the penis beneath this so that the under surface of the scrotal skin cuff was in intimate apposi-

RECONSTRUCTION FOR TRAUMATIC DENUDATION OF THE PENIS AND SCROTUM

REPORT OF A CASE

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DEFECTS exhibiting total loss of the skin covering the penis or scrotum, or both, invariably cause grave concern for the patient and frequently present difficult problems of reconstruction for the surgeon who assumes their correction. Fortunately, these accidents occur rarely, there being thirty-four reports in the literature,¹⁻³⁴ only thirteen^{1, 9, 12, 13, 14, 15, 21, 23, 24, 26, 30, 31, 33} of which are on avulsion of the skin of both the penis and scrotum. The earliest report of complete destruction of the skin of the penis and scrotum is that of Gibbs,³⁴ in 1855. Sixteen years later, Conrad³³ reported a case of reproduction of the scrotum. The remaining reports have all been recorded in the present century. It is interesting to note that with the advent of the more extensive use of machinery, reports of this accident have appeared with increasing frequency.

Defects resulting in complete ablation of skin covering of the penis may be considered either traumatic or infectious. The traumatic group includes those cases in which the loss has resulted from direct trauma, as in accidents^{4, 7, 8, 11, 14, 15, 22, 24, 25, 27, 28, 33} or burns, or surgical trauma, as in circumcision.² The infectious group consists of those cases arising from any infectious process, as lymphogranuloma inguinale² or urethritis.³²

The essential problem in the correction of surface defects of the penis is that of restoration of skin coverage. Surgical reconstruction is modified by the specific type of defect and associated complications. In those cases in which complete loss of skin has resulted from trauma (accidental or surgical), repair can be satisfactorily accomplished following an adequate débridement and the application of a half-thickness skin graft. Restoration of coverage in the infectious case obviously requires more detailed consideration and, naturally, infection must be eliminated first or sufficiently reduced before a graft can be judiciously applied. The defect must be in a state which will not only permit the formation of healthy granulation but which will also support the graft and maintain its viability.

Examination revealed a greatly enlarged and edematous penis. The edematous prepuce was hanging over the meatus. A urethral discharge was present. The testicles were slightly swollen and tender.

A diagnosis of gangrene involving the whole dorsal portion of the skin of the penis and subcutaneous tissues was made, September 5. On the same day, a suprapubic cystotomy was done by the urologist.



Fig. 3.



Fig. 4

Fig. 3 —Photograph showing first stage repair where penis is buried beneath scrotal cuff transplant.

Fig. 4 —Photograph showing healing following application of scrotal cuff transplant. A clear comparison of the results obtained from skin graft and scrotal cuff transplant is seen when comparing Fig. 4 and 7.

tion with the defect over the shaft of the penis. Restoration was successful in this instance and the patient suffered no pain following reconstruction. A report of this case follows.

CASE REPORT

T. B., a 56-year-old negro farmer, was admitted to Charity Hospital, Sept. 3, 1934, on the genitourinary service, complaining of swelling of the penis. Three days before, the penis became swollen rather suddenly. He had had a discharge from the urethra for several weeks. He could urinate only in small streams and complained of a burning sensation following urination.

Fig. 1.

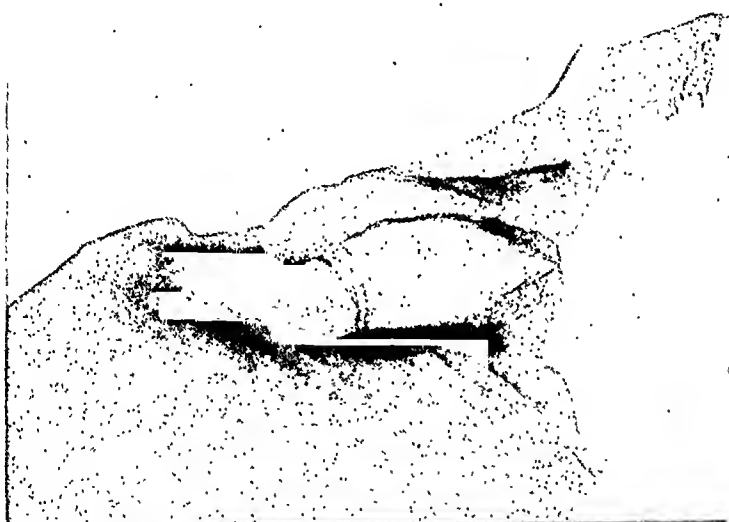


Fig. 2.



Fig. 1.—Photograph showing defect of the penis following infection.
Fig. 2.—Lateral view showing defect of penis following infection.

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Fig 3



Fig 4

Fig 3—Photograph showing first stage repair where penis is buried beneath scrotal cuff transplant

Fig 4—Photograph showing healing following application of scrotal cuff transplant. A clear comparison of the results obtained from skin graft and scrotal cuff transplant is seen when comparing Fig 4 and 7.

On October 10, the patient was seen in consultation. An examination at this time revealed a defect of the penis which extended from the corona to the symphysis pubis and involved the entire dorsum to extend downward on either side practically to the frenum, thus leaving only a small portion of skin extending from the frenum back to the scrotum on the under surface. There was evidence of chronic infection and lymphedema in the skin at the base of the penis, which extended down to be reflected in the skin of the scrotum. The defect under the penis was relatively free of infection and under the entire surface there was a firm, smooth, velvety granulation (Figs. 1 and 2).

It was decided to attempt repair with cuff pedicle skin transplant. A pattern of the denuded portion of the penis was made and an area this size outlined over the anterior surface of the scrotum. Transverse lines were made at the point representing the length of the pattern and the skin was incised along these lines down to the subcutaneous tissues. The skin between the two incisions was then separated from the subcutaneous tissues so as to form a tunnel, through which the penis was drawn. With the penis in this position, the undersurface of the skin of the tunnel was in approximation with the denuded area on the dorsum of the penis. Skin borders at the base of the penis and at the corona were pared and to these pared borders end-on mattress sutures of chromic 0000 silkworm gut were applied. A xeroform dressing was then placed over the wound (Fig. 3).

The cuff took nicely and on October 24, the second stage of the operation was done. Under spinal anesthesia, the right pedicle of the cuff was cut and the edges of the penile skin were freed and the cuff sutured to them. On October 31, under local anesthesia, the left pedicle was cut away and the graft sutured to the skin of the penis after it had been freed. The patient was discharged Jan. 2, 1935, completely healed (Fig. 4).

The end result from a serotal skin flap is not as satisfactory as from the half-thickness skin graft because of the increased thickness and the loss of pliability resulting from the former method.

Because there was complete loss of all serotal skin and because the defect was further complicated by an extensive laceration downward into the perineum extending almost to the anus, reconstruction of the defect of the penis by a half-thickness skin graft was employed in the following case.

REPORT OF CASE

J. H., a white farmer, aged 38 years, was admitted to Charity Hospital, Oct. 6, 1938. Eight hours before, while working on a rice binder, he stepped too close to the drive shaft connecting the binder to a tractor. Not only the clothing but also the external genitalia were caught by a coupling on the shaft, which was revolving at high speed, resulting in complete denudation of the penis and scrotum (Figs. 5 and 6).

Examination on admission revealed a patient lying flat on his back, fully conscious, with no suggestion of shock. The penis and testicles were wrapped in a dressing of old linen, which was saturated with blood. Close inspection revealed a penis completely denuded from the base to the corona, where there was a small cuff of mucosa. All serotal skin was lost. The testicles were freely movable and could be widely separated without difficulty. There was no apparent injury to the cord on either side. Beneath the testicles and extending posteriorly almost to the anus, was a laceration which permitted sufficient separation of skin margins to give a large, exposed perineal wound. There was no apparent involvement of the anus nor perforation of the fascia.

It was obvious that skin graft would not be desirable for complete repair of such an extensive defect (entire loss of the skin of the serotum and penis) because of the inability of adequately applying pressure to hold the skin graft in intimate contact with the total surface of the defect. To attempt to cover the testicles completely by means of single pedicle skin transplant or other types of tissue transplant would have been equally as injudicious. Obviously, satisfactory repair could result only from a procedure which would permit the immediate grafting of the penis and the burial of the testicles under a protective skin covering. Unless this could be accomplished, certain infection with its subsequent complications would ensue. Therefore, the skin was dissected along the medial aspect of each thigh so



Fig. 5.



Fig. 6.

Fig. 5.—Photograph showing complete loss of skin over penis and testicles.

Fig. 6.—Photograph showing complete loss of skin over penis and testicles. Note the complete freedom of the testicles and the extensive lacerated wound shown below the right testicle where it extends deep into the perineum.

as to form a small pocket between the skin and the underlying fat and fascia of the thigh. This was enlarged sufficiently to permit the reception of a single testicle, each being placed in a corresponding pocket on its respective thigh. There was no undue tension nor distortion of the testicles. On the contrary, the pocket seemed to support the testicles so that there was less tension on the cord than is usually seen. The skin border above the pocket was then approximated with the opposite skin border of the defect and held together by means of interrupted sutures of black silk and 0000 silkworm gut. Thus, each testicle was completely encased beneath the skin, medial to the thigh on its respective side, and was covered with skin and a

Fig. 7.



Fig. 8.

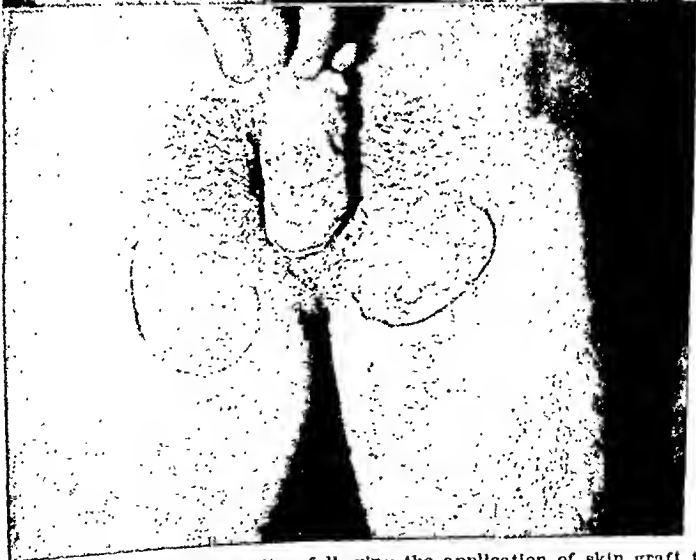


Fig. 7.—Photograph showing healing following the application of skin graft to the penis. Photograph taken approximately three months following operation.

Fig. 8.—Photograph showing complete healing of penis following application of skin graft. This photograph shows the testicles where they are imbedded beneath the skin of the thighs as shown by the outline over the skin of the thighs.

slight padding of fat as a protection. A half-thickness skin graft was removed from the inner surface of the right arm and applied around the entire shaft of the penis. It was held fixed by means of interrupted sutures which completely encircled the skin near the corona and another row of interrupted sutures attaching the skin graft to the abdominal perineal skin at the base of the penis. Sutures were also taken down the line where the longitudinal border of the skin graft overlapped. This held the skin firmly in place around the shaft of the penis. A xeroform gauze dressing was applied over the entire surface of the skin graft. Over this a dry gauze, sea-sponge, pressure dressing was applied. A week later the dressing was removed, revealing a satisfactory graft. There was no evidence of infection around the perineal wound nor in the pockets which had been formed for the reception of the two testicles. The dressing was changed daily thereafter, and on the fourteenth day the patient was permitted to sit up in a chair (Figs. 7 and 8).

On the theory that sterility ensues in a testicle which maintains a temperature equal to body heat and not one degree less, reconstruction of a scrotum was next considered. This could be done by forming a single pedicle skin transplant from the skin of the thigh immediately covering the buried testicle and raising the skin and its underlying fat with the testicle attached so as to bring it into approximation with a similar flap on the opposite side.¹⁴ The two flaps covering their respective testicles would meet and approximate in a cuplike fashion so that they could be sutured around their circumference, thus completely encircling the two testicles and giving absolute skin covering with an underlying fat pad for protection. This, of course, would have necessitated three operative stages. The resulting serotal sac would have been considerably larger than normal and would have been devoid of any contractile property. However, the patient was not even remotely interested in this operation. When confronted with the fact that he would most likely be sterile if some attempt to remove the testicles from their present site was not carried out, he stated that sterility was desirable because of the large size of his family. When last seen and examined, April 1, 1940, the patient was found to be completely healed with satisfactory results. He has experienced no difficulty in any respect and there has been no disturbance whatever with normal physiologic functions.

REFERENCES

1. Agostinelli, E.: Note di falloplastica a proposito di un caso di strappamento della pelle del pene e dello seroto, *Polielinico* (sez. prat.) 46: 1303, 1939.
2. Brown, J. B.: Restoration of the Entire Skin of the Penis, *Surg., Gynec. & Obst.* 65: 362, 1937.
3. Cruickshank, M. M.: Denuded Penis After Operation for Elephantoid Scrotum, *Indian M. Gaz.* 72: 87, 1937.
4. Dune, M. V.: Traumatic Loss of Skin of Penis, *Vestnik. khir.* 53: 51, 1937.
5. Bogoroz, N. A.: Plastic Restoration of Penis, *Sovet. khir.* 8: 303, 1936.
6. Frolov, V. I.: Plastic Reconstruction of the Skin by Filatov Grafts, *Vestnik khir.* 46: 251, 1936.
7. Knntor, A.: Traumatischer Verlust der Haut der männlichen Genitalien. "Schindung" der Genitalien, *Chirurg.* 8: 972, 1936.
8. Takashima, R., and Kusano, M.: Über einen Fall von totalem Defekt der Penishaut durch Maschine, *Zentralbl. f. Chir.* 63: 84, 1936.
9. Sasaki, S.: Schindungsverletzung des Skrotums und ihre plastische Operation (Nachtrag), *Taiwan Igakkai Zasshi* 34: 455, 1935.
10. Dexelmann, J.: Über einen Fall von isolierter Skalpierung des Penis und Skrotums, *Zentralbl. f. Chir.* 59: 2760, 1932.
11. Rihmer, B. von: Traumatische Entblössung des Penis von seiner ganzen Hautbedeckung mit nachfolgender partieller Harnröhrennekrose. Schliessung der Harnröhre. Phalloplastik, *Ztschr. f. Urol.* 26: 369, 1932.
12. Rihmer, V. von: Phalloplasty; case, *Budapesti orvosi ujság* 30: 73, 1932.
13. Turschmid, W.: Traumatic Avulsion of Skin of the Penis and Scrotum, *Polska gaz. lek.* 11: 373, 1932.
14. Robertson, J. F.: Avulsion and Reconstruction, *South. Med. & Surg.* 93: 527, 1931.

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Fig. 7.

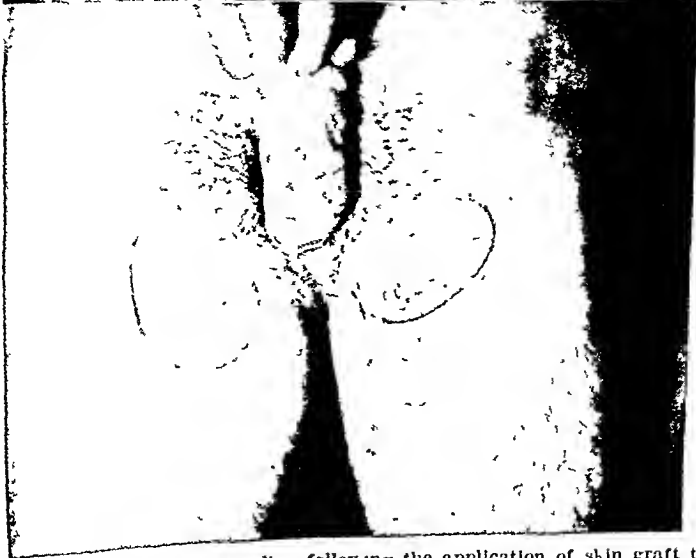


Fig. 8.

Fig. 7—Photograph showing healing following the application of skin graft to the penis. Photograph taken approximately three months following operation.

Fig. 8—Photograph showing complete healing of penis following application of skin graft. This photograph shows the testicles where they are imbedded beneath the skin of the thighs as shown by the outline over the skin of the thighs.

THE ELEVATION OF THE NASAL BRIDGE LINE

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INTRODUCTION

FOR centuries the stigma of a misshapen nose has caused the bearer to seek relief of his deformity either through surgery or through the camouflage of a corrective cosmetic make-up. In the early middle ages, artificial noses were often worn by normal people as a stylish fetish. Therefore, little comment was caused when those with nasal defects wore these same artificial noses to cover their deformities. In this age the so-called "fathers of plastic surgery" rose to fame, not by their ability to reconstruct an ear or to graft an unhealed area, but primarily on the self-heralded excellence of their nasal reconstructions. Their claims of success became so fantastic that they excited the ridicule and disbelief of both the church and the public, so that by the late eighteenth century the whole field of reconstructive surgery had fallen into great disrepute. Such a stage of indignation over charlatan claims and practices was reached that the Paris Faculty in 1778 passed a resolution forbidding any further corrective surgery of the face.

Since that time the scope of plastic surgery has widened to include the relief of many conditions other than nasal deformities. The principles governing this field of surgery have been founded gradually and, contrary to popular belief, were well established long before World War I. Several procedures were tested during this war which resulted in the popular adoption of many of the sound procedures and the discontinuation of most of the unsound ones. These principles have been embellished further during peace time so that now they have attained significant stature among the surgical fundamentals for World War II.

CAUSES OF NASAL DEPRESSION

Congenital.—The external portion of the nose is formed by a central field of tissue that curves down over the head of the embryo and advances caudally on the ventral surface until it meets the paired maxillary protuberances from the first branchial arch to form the upper lip. This central cranial field, more commonly called the nasal field, is made up of four anlage, a central pair bounded on each side by another which

- ✓15. Counseller, V. S., and Palmer, B. M.: Avulsion of Skin of Penis and Scrotum, *S. Clin. North America* 9: 993, 1929.
16. Kenny, T. B., and Merello, M.: Arrancamiento traumatico de la piel de pene y del exocroto. *Tecnica operatoria de la genitoplastia reparadora (exocroto—peniana)*, *Presna méd. argent.* 15: 1549, 1929.
17. Meyer, H.: Phalloplastik nach Schindung, *Arch. f. Orthop.* 27: 437, 1929.
18. Vadi, E.: Cirugia plástica. Presentación de un caso, *Bol. Asoc. méd. de Puerto Rico* 22: 25, 1929.
19. Koch, K.: Missglickter Versuch gestielter Plastik aus dem Skrotum, *Zentralbl. f. Chir.* 55: 587, 1928.
20. König, E.: Plastischer Ersatz des Hodensackes, *Arch. f. klin. Chir.* 150: 244, 1928.
21. Buzzi, A., and Saravia, E. C.: Resultados de una plastica del pene, *Rev. de cir.* 6: 662, 1927.
22. Cottle, G. F.: Avulsion of Scrotum, Left Testicle and Sheath of Penis, *U. S. Nav. M. Bull.* 20: 457, 1924.
23. Stirling, W. C.: Case of Gangrene of Scrotum and Penis, *J. A. M. A.* 80: 622, 1923.
24. Aspinall, A.: Complete Avulsion of Skin of Scrotum and Penis, *M. J. Australia* 1: 502, 1918.
25. Welch, K.: Avulsion of the Skin of Scrotum and Penis, *M. J. Australia* 1: 527, 1918.
26. Carr, W. P.: Plastic Operation for Restoring Scrotum With Report of Case, *Am. J. Dermat. & Genito-Urin. Dis.* 25: 292, 1911.
27. Westbrook, R. W.: Complete Avulsion of Integument of Scrotum and Penis, *Long Island M. J.* 5: 405, 1911.
- ✓28. Powers, C. A.: Complete Denudation of the Penis, *Ann. Surg.* 49: 238, 1909.
29. MacDonald, J. A.: Plastic Operation for Complete Loss of Scrotum, *Indiana M. J.* 26: 227, 1907.
- ✓30. Weeks, L. C.: Ablation of the Scrotum, *Northwest. Lancet* 25: 91, 1905.
31. Wood, A. C.: Complete Avulsion of the Scrotum, Left Testis and Skin Covering Penis, *Am. J. Dermat. & Genito-Urin. Dis.* 9: 196, 1905.
32. Guiteras, R.: A Plastic Operation for a New Scrotum With Report of a Case of Gangrene and Slough of the Integument Over the External Genitals, *J. Cutan. & Genito-Urin. Dis.* 20: 211, 1902.
- ✓33. Conrad, A.: Reproduction of Scrotum After Injury, *St. Louis Cour. Med.* 6: 41, 1881.
- ✓34. Gibbs, R. W.: A Case Where the Entire Scrotum and Perineum Together With One Testicle and Its Cord Attached and Nearly All the Integument of the Penis Were Torn Off. Recovery With Preservation of Sexual Powers, *Charleston M. J. & Rev.* 10: 145, 1855.

which a hematoma, particularly of the septum, is allowed to remain untrained so that it subsequently becomes infected. An osteomyelitis of the nasal bones is the frequent sequelae with either absorption or extru-



Fig 1



Fig 2

Figs 1 and 2 (Case 1)—This patient exhibits a congenitally small nose with the deficiency particularly marked at the nasal bridge. She was observed over a period of two years during which time there was no improvement. At the age of six years a hinged osteochondral graft was inserted.



Fig 3



Fig 4

Figs 3 and 4 (Case 1)—Photographs taken two years after insertion of the hinged osteochondral graft. There has been definite growth of the graft in proportion to the rest of the body growth.

together make the lateral pair. The central pair form a portion of the dorsum of the nose, a portion of the nasal septum, the columella and filtrum of the lip. The lateral pair develop into the sides of the nose and the alae.

If there is an absence of the entire nasal field, the patient is born with no nose at all. If there is an arrest in its descent, the nose is represented by two nostrils up above or between the eyes. If one lateral nasal process fails to descend, the patient will be born with only one nostril.

If the descent of these processes progresses in the normal manner but the amount of tissue contributed by each is deficient, the result is a perfectly formed nose except that it is too small. A patient with this anomaly characteristically has a very flat nasal bridge, epicanthal folds, and a turned up nubbins of soft tissue perforated with normal nostrils representing the tip. It is this latter type of deformity that is ordinarily neglected when the patient is a child because of the erroneous idea that it will correct itself. This results in a young adult with a nose many sizes too small for the rest of the face. It is very difficult to correct the deformity in adult life because the soft tissue, deficient to begin with and never having been stretched by proper bone growth beneath it, is incapable of being distended to the proper size in one operative maneuver. It is my opinion that an osteochondral graft from the crest of the ilium should be inserted when the patient is 4 or 5 years of age in an effort to stretch this skin early in life. If the graft takes properly it should presumably grow with the patient, as is shown in Case 1. If the result is satisfactory when the patient reaches 15 or 16 years of age, further operative procedures will not be necessary. If it is not satisfactory, this first graft can either be added to, or removed and replaced with a larger graft at this time. The procedure of grafting early should produce gradual stretching of the skin covering so the insertion of a graft of adequate size can more easily be accomplished when the face has reached adult proportions.

Neoplastic.—Tumors involving the nose, like those elsewhere on the body, may be either benign or malignant. Benign tumors, such as hemangiomas or lymphangiomas, are usually eradicated by radiation or excision without the destruction of the bony framework. Malignant tumors may involve bone and thus require excision of the entire nose including the bony and cartilaginous framework to remove the tumor successfully. In the latter case an entire nose must be rebuilt, a procedure which does not come within the scope of this paper. Benign tumors of the septum, such as a dermoid, may be so extensive that removal of all or part of the supporting structures may be necessary for extirpation of the growth. The late result may be either a depressed nasal bridge or tip which will require elevation with a graft for a good cosmetic effect.

Infections.—Infections frequently follow trauma to the nose in which there has been a compound fracture of either bone or cartilage, or in

Trauma.—Fractures of the supporting framework of the nose are frequent and are accompanied by varying degrees of displacement of these structures. Unless the comminution of the fragments is excessive, all of the parts that are displaced usually can be restored to their original positions soon after the injury without the necessity of using a graft for additional support. However, if the trauma has been frequent and repeated at intervals over a prolonged period of time, simple refracturing and restoration of the bone and cartilage to their normal positions often is not sufficient to produce a good cosmetic result. These old fractures are characterized by a flattening of the entire nasal bridge in addition to a crushed and badly deviated septum which is



Fig. 7.



Fig. 8.

Figs. 7 and 8 (Case 2).—Photographs taken eight months after insertion of a single wedge-shaped bone graft from the iliac crest without the use of the septal hinged portion.

not able to be permanently raised or straightened. In the latter case it is preferable to perform a submucous resection of the distorted septum and, possibly during the same operative procedure, to refracture and set the nasal bones into as nearly normal a position as possible. After a six-month interval further elevation of the bridge line can be accomplished by the insertion of a graft. In some patients whose features are naturally large, the flattening of the nasal bones may be so marked that it is frequently more satisfactory to build a broader nose by inserting a wide graft without the preliminary refracturing (Case 4).

sion of the bone as sequestra. Infection of the hair follicles within the nasal vestibule may extend to the septum to cause destruction of the cartilaginous portion of the septum and occasionally the bony framework. For centuries, lupus and syphilis have been classic in producing nasal deformities which were so distinctive that they were easily recognized even by laymen.



Fig. 5.



Fig. 6.

Figs. 5 and 6 (Case 2).—This patient received a crushing injury to his nose which resulted in a compound fracture of the nasal bones and septum. Following this he had an infection of the septum (cartilaginous) which subsided after drainage. These photographs were taken one year after the injury.

The successful treatment of nasal destruction following infection depends upon the complete control of whatever infectious organisms caused the original deformity. Syphilis and lupus must, therefore, be well bridled before reparative measures are begun. To allay the danger of reactivating an old infection it is always a wise precaution to wait at least six months to a year after an acute infectious process has subsided before proceeding with operative reconstruction. It is also necessary to evaluate exactly what tissues have been lost before the repair is begun. If a significant portion of either the nasal skin or the nasal mucosa has been destroyed in addition to the bony or cartilaginous support, no amount of stretching of the remainder by means of a graft will produce a satisfactory result. In the latter case a lined pedicle flap from the forehead, arm, or acromipectoral region is brought up to replace the loss of soft tissue and at a later date the supporting structure is inserted.

substances under the nasal skin. Of these, the most widely used was a wax of low melting point which was injected in the subcutaneous tissue over the nose, moulded in the proper shape with the fingers, and set by the application of cold packs. The effect was only temporary, the usual termination being either a slough of the nasal skin or a paraffinoma. It is unfortunate that this method is still used by less reputable men and some licensed cosmeticians. Other inert substances such as silver, celluloid, and ivory, when cut to the proper shape, have been and are still used. These artificial supports have usually caused the surrounding tissues to react in such a fashion that extrusion of the foreign body was inevitable.



Fig. 13.

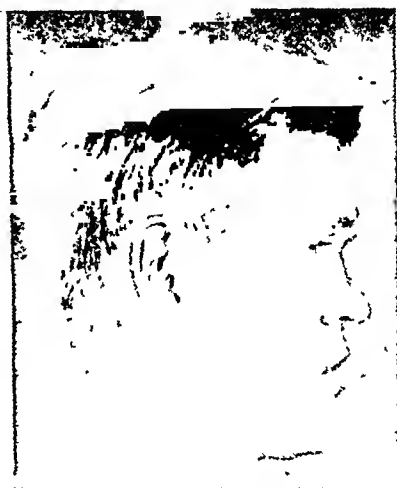


Fig. 14

Figs. 13 and 14 (Case 4) —Photographs of a patient who had had his nose fractured on five different occasions in eleven years. The last injury occurred two years before these pictures were taken.

Autogenous grafts of fat or fascia have been employed with varying degrees of success. A sufficient residue of either tissue is difficult to maintain, as uncertain proportions of both substances tend to melt away gradually when transplanted out of their usual environment. Through trial and error, the materials insuring the best and most permanent results have been found to be either bone or cartilage. The autogenous grafts of both of these substances are used by the majority of plastic surgeons, but recently preserved homogenous grafts of cartilage have been found to be equally successful.*

The author has found that the use of autogenous cartilage grafts has one important disadvantage to offset the obvious advantage of working with a material that may be easily shaped to the desired contour. The only donor site of autogenous cartilage of the desired

*C. L. Straith, and W. B. Slaughter, M.D., Grafts of Preserved Cartilage in Restoration of Facial Contour, J. A. M. A. 116: 2008-2013, 1941

CHOICE OF MATERIALS

The methods of elevation of the depressed nasal bridge line have run the plastic gamut perhaps more than any other reconstructive procedure. After the passing of the era of artificial noses, attempts were made to fill up a nasal depression by the insertion of various nonviable



Fig 9



Fig 10

Figs 9 and 10 (Case 3) —Photographs taken fourteen years after an operation for a deviated septum. At that time either too much of the septum was removed or the patient developed a hematoma that became infected and resulted in this depression.



FIG 11



Fig 12

Figs 11 and 12 (Case 3) —Photographs taken two years after insertion of a hinged bone graft taken from the crest of the ilium.

The desired amount of bone necessary for this reconstructive work is more easily available than is a similar amount of cartilage and may be procured from either the iliac crest, tibial crest, or ribs. The only distinct drawback encountered with the usage of bony struts is the difficulty in handling and carving it to the desired shape. This latter difficulty may be overcome by use of the proper instruments and the development of an operative technique which is suitable. It has been my experience that bone from the iliac crest has served admirably to relieve nasal deformity without any sequelae that were distressing to either the patient or surgeon.

TECHNIQUE OF OBTAINING AND USING ILIAC BONE

On the evening before operation the hairs inside both nostrils are clipped and the nasal vestibule cleaned with swabs of normal saline solution. The face is then thoroughly washed with mild soap and water and swabbed with a weak astringent solution. In women, the use of face creams usually applied upon retiring is forbidden. The pubic area, lower abdomen, and upper thighs are shaved and cleansed in the same fashion as the face. These fields are not wrapped in sterile towels, as I believe that this practice produces an excess in perspiration, thereby raising the local bacterial count. On the following morning all fields are again cleansed in the same fashion as they were the night before, except that for men a complete close shave of the face is done two hours before operation.

Although the entire operation is possible under a local anesthetic to the nasal area and a spinal anesthetic for the hip area, I advise a general anesthetic, preferably rectal avertin supplemented with intratracheal gas-oxygen ether. A general anesthetic eliminates any psychic distress due to the noise and pressure caused by the chiselling of the bone from the iliac crest.

At the time of the operation the fields are again prepared with soap, water, alcohol, and ether. The inside of the nose is carefully swabbed with some mild nonirritating antiseptic such as zephiran or aqueous merthiolate. The distance is now measured off from the glabella to the apex of the nasal tip, a point formed by the anterior reflexion of the alar cartilages on the septal cartilages. These two points are marked with Bonney's blue paint and the midline of the nose between these points is dotted on the skin with a sharp fine needle dipped in the same dye. If only a single straight wedge-shaped graft is to be used without a columellar strut this glabella-to-tip measurement will then represent the length of the desired bony segment. If a columellar strut is needed to insure support of the tip, then this measurement represents only two-thirds of the length of the required amount of bone.

A solution of eight drops of $\frac{1}{1,000}$ adrenalin to the ounce of either saline solution or novocain is injected next into the columella, the

quantity necessary for raising the nasal bridge is situated at the juncture of the anterior ribcage with the sternum. All of these cartilages are naturally curved. In order to fashion a straight segment from this tissue it is necessary to whittle it down at both ends and leave the middle relatively undisturbed. Microscopic examination of the finished cartilaginous strut, even though straight externally, will show that the predominance of cells still run in a curved direction. When this support is placed under the nasal skin it will appear at first to be straight but as time goes on, an appreciable number of grafts will begin to twist and re-establish the original curvature that existed in the donor sites. It has been stated that preserved homogenous grafts have less of this distressing tendency toward the development of curvatures subsequent to operation, than either homogenous or autogenous fresh cartilage.



Fig. 15.



Fig. 16.

Figs. 15 and 16 (Case 4) — Photographs taken one month after insertion of a hinged bone graft from the crest of the ilium. The entire width of the iliac crest was used to fashion a wide enough graft so that the new nose would match the other rugged features in this face.

When bone is properly used for nasal support this disadvantage of late curvature is eliminated. Some authors have reported gradual absorption of calcium from the bony framework in this site and the replacement of it with fibrous tissue. However, this fibrous tissue replacement has usually been in quantities sufficient to retain the original cosmetic effect so that the loss of calcium is of little importance. This absorption has not taken place in those cases in which the graft was inserted in such a fashion that bony union between the graft and the nasal bridge was the effect wished for and obtained.

silk sutures to the muscle and fascia layers, subcutaneous layer, and subcuticular layer. A continuous suture of fine dermic is used for the skin. A small rubber wick drain is inserted down to the bone to remain in place for twenty-four hours. A pressure dressing of gauze, elastoplast, and A-S-E bandage is then applied.

The bone removed from the ilium is now sculptured to the desired size and shape. This part of the procedure is the most difficult and exasperating of the entire operation. Unless the instruments used for holding the graft are adequate, the graft is likely to skid off the table. If the instruments used to mold it are dull, it may be broken or crushed out of its planned shape.

If a single bridge strut is to be used, the shape of the graft on antero-posterior view is roughly rectangular, the end of the rectangle which will lie at the nasal tip being slightly narrower than that which will lie at the glabellar end. On the lateral or profile view, this graft is thin in the glabellar region, reaches the limit of its thickness at the point where the graft will leave the support of the nasal bones on which it is to rest, and again gradually thins toward the tip. In this view the part that will form the bridge line is straight, so that one can imagine the graft to be shaped like a solid triangle, the base being the bridge line, one side the portion that will rest on the nasal bones, and the other side the part that extends from the nasal bones to the tip of the nose. The apex or peak of the triangle rests at the point where the graft leaves the support at the anterior end of the nasal bones. The under surface of the side that rests on the nasal bones is grooved slightly down its center to fit tightly to the slight transverse curvature of the nasal bones.

If a columellar strut is needed in addition to the bridge support, a segment of bone one-third longer than that required for a single wedge graft is removed. The bridge portion is formed in the same fashion as that described above but the periosteum of the graft is left intact at the tip end to serve as a hinge for the narrow columellar portion. The columellar portion folds back on the hinge so that the intact periosteum forms an angle of 270° at the tip. Further support of the tip is effected by the upper end of the body of the columellar strut which rests against the slanting under surface of the tip of the bridge portion for a distance of about 1 cm.

After the graft has been cut to the desired shape, the pack is removed from the nose slowly and carefully, to prevent hemorrhage. Two skin hooks are placed in the skin to hold the incision apart while the graft is inserted. It is absolutely necessary that the graft be placed inside and not above the periosteal pocket made to receive it. If the graft has been correctly shaped by measurement it will fit tightly and securely without any tendency to shift or twist out of position. When a columellar prop is used the free end must fit snugly onto the maxillary mens in order to give stability to the tip. The columellar wound

septum, and beneath the periosteum of the nasal bones. This will facilitate both the dissection and the control of hemorrhage. A vertical incision is made through the skin of the columella, dividing it into two longitudinal halves. To prevent perforation of the septal mucosa a forefinger is inserted in one nostril and the thumb in the other; the lower septum is held between the two while the skin incision is deepened by sharp dissection until the knife reaches the nasal bones. The operator then changes the glove on the hand that held the septum and packs each nostril with a swab soaked in a mild antiseptic solution. The knife is again inserted and the periosteum of the nasal bones is cut transversely at its anterior attachment with the bones. A periosteal elevator is then inserted through the columellar incision, and guided through the transverse incision in the periosteum, where it is pushed upward carefully in order to raise the periosteum off the bones and create an oblong pocket all the way up to the glabella. After this pocket has been formed, the outer table of the nasal bones are scraped with a file to give a better foundation for the graft. The entire cavity thus formed is now packed with dry gauze to control hemorrhage. Care must be taken in placing this pack to prevent distention of the skin to the point of shutting off the circulation to the relatively thin layer over the bridge line. A pack of iced sterile saline solution is placed over the outside of the nose to help control hemorrhage and to prevent excessive edema. It must be emphasized that this dissection should be done most gently and carefully, with the tips of the fingers of one hand always placed on the external surface of the nose over the point where the instrument is being used. This is the only safe way to prevent tearing through or "buttonholing" the skin over the bridge line.

An incision is now made over the iliac crest so that the inferior end of the incision terminates at the anterosuperior spine of the ilium. The incision is carried down to, but not through, the periosteum. The attachment of the muscles is freed from the lateral border of the crest for the entire length of the incision and for a depth of about one inch. Bleeding is usually controlled by retraction of the cut muscle ends under pressure. The desired length of bone is now measured off on the iliac crest. Usually the ilium is of sufficient thickness so that only a portion of the crest and outer table is needed. Occasionally a wide nasal bridge is required so that a segment comprised of both the inner and outer tables is removed in one piece (Case 4).

The procedure of removing this segment must follow a strictly "no-hand-touch" technique. Separate instruments and instrument tables are used to avoid any possible contamination of the raw bone with the gloved hands that have come in contact with the external skin. The bony fragment is chiseled away from the crest and is then dropped into sterile saline solution while the donor site is closed. The closure is in three layers with either interrupted fine catgut sutures or fine

COTTON SUTURE MATERIAL AND EARLY AMBULATION IN GYNECOLOGY AND OBSTETRICS

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IN RECENT years there has been a decided trend in surgical practice toward adoption of nonabsorbable suture materials in most fields of endeavor, and of these, silk has been the most widely used. Even more recently, however, stimulated by the reports of Gage, and Meade and Ochsner, spool cotton has acquired prominence. Each month new reports confirm the original observations justifying the use of cotton and indicating its ever-widening acceptance. In gynecologic surgery the swing toward nonabsorbable materials has been less enthusiastic, largely because of prejudice born of misuse of the materials employed. In July, 1941, a clinical trial of spool cotton was instituted in selected cases on the colored gynecologic service, Tulane Unit, Charity Hospital, New Orleans. Results in these first few cases were so gratifying that the scope was rapidly broadened until, at present, cotton suture material is used exclusively by us in all gynecologic operations. We now have complete data on 160 cases, and it is our purpose to report the results in these cases.

Needless to say, in changing from catgut to cotton sutures, our technique had to be altered completely, and parenthetically, considerably improved. Cotton, like any other nonabsorbable suture, when used according to the principles of Halsted, calls for an exactness of technique, no longer the mass crushing and ligation of tissue, with its inevitable tissue necrosis. At first this change was difficult and it seemed almost necessary to continue our former methods of handling the tough ligamentous and scarred tissue. With increased experience, however, we found it simpler to deal with smaller bits of tissue and employ lighter suture material. When our study commenced, for instance, crochet cotton No. 20 was used to ligate the uterine and ovarian vessels; this was quickly reduced to No. 8. Now we are able to perform total hysterectomy with no suture material heavier than No. 40 (ordinary sewing cotton). In plastic work we have reduced the size of our sutures to No. 80 and No. 120, almost incredibly fine in diameter, but with sufficient tensile strength for the purpose. We have found that the average increased

is now closed by sutures of 4-0 plain catgut to the subcutaneous tissue, and the skin approximated with sutures of 8-0 dermic. Whitehead's varnish is painted on the wound, over which is placed a one-half inch gauze tape that will become adherent to the wound when the varnish becomes dry enough to be tacky.

POSTOPERATIVE CARE

For the first forty-eight hours after operation constant sterile iced saline solution compresses are kept over the nose and eyes. Any accumulation of blood in either the donor or recipient areas must be immediately expressed or aspirated to prevent infection and residual thickening in these sites. The skin sutures are removed from the columella on the third or fourth postoperative day and those from the donor wound on the seventh postoperative day. The patient's nostrils are carefully oiled each day and kept free of crusts. When the edema begins to subside on the third or fourth postoperative day the mucosa may be shrunk even further with sprays of ephedrine sulphate. This is done primarily for the patient's comfort and to prevent sneezing or coughing. Both of the latter acts, if violently done, may start up a secondary hemorrhage in the periosteal pocket. The patient is allowed to walk about on the eighth or ninth postoperative day, at which time he usually complains of muscle soreness in the hip region. This soreness generally disappears after a few days of graduated exercise so that the patient can resume normal work two to three weeks after operation.

The graft becomes firmly adherent by bony union to the nasal bones within six to eight weeks. X-rays taken at this and subsequent times show moderate loss of calcification comparable to that which would occur in any bone of the extremities after a period of six to eight weeks of nonuse.

The result may now be considered permanent, because if primary healing is good, subsequent absorption does not occur. Further evidence of the fact that this graft is viable is proved by one of the cases treated by Gillies* in which the bone graft was fractured by a blow to the nose several months after implantation. Simple setting of this fracture of the graft was done. After six weeks the two fractured ends of the graft had healed in good position with the resumption of the previous excellent cosmetic result.

CONCLUSIONS

Bone grafts taken from the iliac crest and inserted in the nose for the purpose of raising the bridge line or giving support to the nasal tip have produced satisfactory results without extrusion, destruction, distortion, or absorption of the graft at a later time. Specific technical details for obtaining, shaping, and inserting this type of graft have been outlined, together with indications for its use.

*Sir Harold Gillies: Personal communication.

Our results in plastic procedure are even more gratifying. Here again, we have been reassured by excellent functional and cosmetic results, lowered morbidity and postoperative comfort. As with the laparotomies, the patients are ambulatory in perfect comfort. It is almost in the realm of fancy to see patients who have had such operations as vaginal hysterectomies and repair of third-degree lacerations, walking and sitting at ease within twenty-four to thirty-six hours after operation. In several instances patients thought that the operation had not yet been performed. This is attributed mainly to lack of tissue reaction resulting from cotton sutures and gentleness in technique. Patients who have had vaginal hysterectomy can be comfortably examined three days after surgery; there is a noticeable lack of discharge, perineal edema, and reaction about the sutures. Again, it must be emphasized that this will follow only after careful surgical technique, especially the inclusion of but small bits of tissue in any one suture, and the use of only fine sutures. Among our plastic procedures, healing was per primam in 100 per cent of the cases, with the exception of one fresh third-degree laceration which evinced a small fecal fistula at the top of the repair. In this instance there was no infection and the poor immediate result is attributed to an omissive error in the repair. The fistula closed spontaneously four weeks following operation. Infection has not occurred in any of our plastic procedures. Table I contains a list of the types of cases in which cotton has been successfully employed.

TABLE I

CASES IN WHICH COTTON SUTURE MATERIAL HAS BEEN SUCCESSFULLY EMPLOYED

Hysterectomies	97	{ Total abdominal	69	71.1%
		{ Supracervical	6	6.2%
		{ Vaginal	22	22.7%
Laparotomies	36	{ Including suspensions, correction of inflammatory conditions, ectopic pregnancies, associated with various plastic procedures.		
Third degree lacerations	6	{ Two fresh, four old, two associated with vaginal hysterectomy.		
LeFort colpoelisis	3			
Secondary repair of wound disruption	4			
Manchester	3	(Two with cervical amputation)		
Anterior and posterior colporrhaphy	2			
Cervical amputation	3	(Sturmdorf, two; Schroeder, one)		
Watkins interposition	1			
Vesicovaginal fistula	1			
Inguinal hernia	1			
Caruncle	1			
Episiotomy	2			

In addition to the above cases, there have been many more episiotomies on our obstetrical service (now done routinely with cotton No. 80 to No. 150 on all cases), the detailed reports of which are not yet available. All of these episiotomies have been uncomplicated during the hospital stay and from the results so far seen in our follow-up clinic we feel that

operating time is about twenty minutes, which would be expected with the use of interrupted sutures, but we feel that this time is well spent, as borne out by the encouraging results that follow.

Among the 115 abdominal incisions there was no single case of serious wound infection, which is noteworthy considering that practically all of the patients were of the lower class, and that the majority were so-called "dirty cases." There was a gross incidence of slight wound infection, which did not interfere with convalescence, in 8.5 per cent including two cases in which subfascial drains were used at the time of surgery as a precautionary measure. In these two cases there was rupture of fresh tubo-ovarian abscess with peritoneal soiling. In no instance was the peritoneal cavity drained. At first this figure may appear to be high but when it is considered that all of our incisions are placed in the mid-line, arising at the umbilicus and terminating the pubic hair area, which is too often inadequately prepared, we feel that the figure is exceptionally good. Miller quotes an incidence of roughly 20 per cent following abdominal hysterectomy on the combined colored and white Tulane University Services at Charity Hospital during 1939 and 1940.

We believe that we have subjected cotton sutures to a rigid clinical test on our service because of the routine postoperative handling of our patients. All operated cases have a standing order granting bathroom privileges within the first twenty-four hours after surgery. Those patients who do not walk on the evening of the operation are escorted to the bathroom the following morning, remaining ambulatory thereafter. Of course, there are occasional exceptions to this rule, but these should be classed as infrequent and specified exceptions, such as peritonitis and pneumonia. Among the 115 laparotomy operations there were sixty-nine patients with total hysterectomies, the majority of which had one or both adnexa removed in addition to appendectomy in 52 per cent, plastic in 4 per cent, and umbilical hernioplasty in 3 per cent. Stay or retention sutures were never used. As stated previously, there was no incidence of serious wound infection, no wound disruption, and in the follow-up there has been no incidence of incisional hernia, to date, among the cotton cases. It might be mentioned here, that while this study was in progress, there were three instances of noninfected abdominal wound disruption among nonambulatory white patients and one colored patient in whom chromic catgut was used. All of these were secondarily closed with cotton sutures and healed uneventfully with exception of the one colored patient, who died in bed the next day of pulmonary embolus.

Our success in early ambulation, together with improved wound healing, is not attributed entirely to cotton. All patients have routine serum protein determinations and are administered blood or plasma until this figure is normal. Cevitamic acid is administered routinely in large doses pre- and postoperatively.

The patients exhibiting positive blood serology for syphilis showed no difference in their convalescence, except that the 7.1 per cent incidence of small granulations at the roof of the vaginal vault following total hysterectomy at six weeks, all occurred in syphilitic cases. Of the vaginal hysterectomies, 9.5 per cent (two cases) showed granulation; 50 per cent of these were syphilitic. This granulation disappeared within four weeks after topical application of silver nitrate. Of course the same type of granulation tissue in the vaginal wall is seen following the use of catgut in a similar operation.

Among the third-degree lacerations, it might be mentioned that one patient weighed 280 pounds and had a vaginal hysterectomy together with Ristine-Nobel repair of a previously repaired third-degree tear. This patient was ambulatory within twenty-four hours and had a 100 per cent functional and cosmetic result.

Criticism may be made regarding the early ambulation of our patients. This practice was stimulated by our previous incidence of thrombophlebitis and pulmonary embolism. Several European authors have described the successful employment of early ambulation, and more recently Ochsner and DeBaKey have recommended its use in the prevention of these complications. While our series is yet small, we have confidence that we will be successfully rewarded in our efforts to prevent these two major postoperative complications. In addition, we have observed a much more rapid convalescence, absence of postoperative weakness, quicker return of bowel and bladder function, and lessened morbidity in general. Without the assurance of nonabsorbable sutures we would be reluctant to allow patients out of bed so quickly.

It has been our practice to leave in situ all sutures used in plastic work in order to determine the fate of these sutures. We have observed them in the follow-up clinic over a period of six months; the knots remain visible and there is no reaction at the site of the sutures. Some of these sutures are undoubtedly shed, but the patients are unaware of their presence or passage.

SUMMARY

1. We have presented data from 160 successive gynecologic operations, wherein cotton suture material has been employed exclusively.
2. Results obtained have more than justified the use of this material as indicated by wound healing, cosmetic results, and postoperative comfort, all largely explained by lack of tissue reaction.
3. We have not felt handicapped by working with cotton as shown by the high incidence of complete hysterectomy (94 per cent) as opposed to supracervical hysterectomy (6 per cent).
4. We recommend the wider use of cotton suture material in gynecology, following the tenets of Halsted, and suggest early ambulation of postoperative patients in the absence of any distinct contraindication.

cotton will survive as a suture of choice in this procedure. In all instances there has been notable freedom from incisional discomfort, as indicated by the fact that all patients are instructed to return to the postpartal clinic for examination and insertion of pessary where indicated as soon as the lochia stops. One of us (C. G. C.) has used cotton sutures with excellent results in episiotomies, plastics, vulvectomy, vesicovaginal fistula, and total abdominal and vaginal hysterectomies, in his private work.

Our results in the larger groups of cases are presented in Table II.

TABLE II

OPERATION	TOTAL	HYSTERECTOMY	SUPRACERVICAL HYSTERECTOMY	VAGINAL HYSTERECTOMY	LAPAROTOMIES	ANTERIOR AND POSTERIOR PLASTICS	LEFORT	MANCHESTER	THIRD-DEGREE LACERATIONS
Number of cases	69	6	22	36	2	3	3	6	
Mortality (%)	2.81	0	0	0	0	0	0	0	
Morbidity (%)	24.6	33.3	22.7	27.7	0	33.3	0	33.3	
Average hospital stay (days)	9.6	9	9.5	7	6	8.3	7.3	11.5	
Increased hospital stay (%)	11.5	0	15.4	0	0	0	0	0	
Positive serology (%)	36.2	20	13.6	22.8	0	0	0	16.6	
Catheterization (%)	39.1	0	54.5	27.7	0	0	66.6	50	
Cystitis (%)	18.8	16.6	36.3	8.5	0	33.3	0	0	
Slight wound infection (%)	10.1	0	0	5.5	0	0	0	0	
Stitch abscess (%)	2.8	0	0	0	0	0	0	0	
Serious wound infection	0	0	0	0	0	0	0	0	
“Cold” (%)	7.2	0	4.5	0	0	0	0	0	
Pneumonia (%)	0	0	4.5	0	0	0	0	0	
Infected cuff (%)	4.3	0	4.5	0	0	0	0	0	
Peritonitis (%)	2.8	0	0	0	0	0	0	0	
Pulmonary embolus	0	0	0	0	0	0	0	0	
Thrombophlebitis	0	0	0	0	0	0	0	0	
Hematoma (%)	1.4	0	4.5	3.7	0	0	0	0	
Postoperative bleeding (%)	0	0	4.5	0	0	0	0	0	
Fistula	0	0	0	0	0	0	0	0	
Follow-up (%)	98.5	33.3	54.5	55	2	100	66.6	83.3	

The two deaths in the total hysterectomy series were both due to *Bacillus welchii* peritonitis, proved at autopsy. The source of infection could not be positively traced. One patient was operated upon for large fibroids and carcinoma in situ of the cervix discovered on microscopic examination; this patient died six days after operation. The other patient had a badly infected cervix and extensive pelvic disease; she died forty-eight hours postoperatively. While both patients had an appendectomy, nevertheless, it is felt that the cervix was the source of contamination. Aerobic and anaerobic culture studies of our suture material failed to show any growth, excluding this possible source of contamination.

INTRATHORACIC ESOPHAGOJEJUNOSTOMY FOR TOTAL GASTRECTOMY WITH LOWER ESOPHAGECTOMY FOR CARCINOMA

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TOTAL gastrectomy has become a more common procedure in recent years. The morbidity and mortality statistics of this operation are also improving steadily. Therefore, it seems advisable to attempt this procedure more often in indicated cases.

Similarly, operations for carcinoma of the cardiac end of the stomach and lower esophagus are being successfully developed. Larger series of intrathoracic esophagogastrostomies are reported.

At the recent meeting of the American Association for Thoracic Surgery held in Toronto, in June, 1941, several papers were read on carcinoma of the esophagus. Wookey, of Toronto, presented cases of successful operations for carcinoma of the cervical portion of the esophagus.

Hence, all the portions of the esophagus and stomach are now becoming more amenable to radical surgical resection.

Recently we had occasion to perform a total removal of the stomach together with the lower two inches of the esophagus, both of which were involved in a linitis plastica type of carcinoma. Reconstruction was accomplished by an intrathoracic esophagojejunostomy.

The patient survived the operation. Death, five months after the operation, was due to general carcinomatosis. Various lessons were learned from this case and therefore it seems worth while to publish these experiences, hoping it may encourage others to attempt the same procedure. Progress will only come in this field if we learn and profit by the experiences of others.

After a careful study of the published literature, it has been found that this case is apparently the first one of a successful intrathoracic esophagojejunostomy. Churchill, of Boston, reported a somewhat similar operation during the discussion at the Toronto meeting of the American

This case was presented before the joint meeting of the Philadelphia Academy of Surgery and the New York Surgical Society on Feb. 12, 1941. It was also reported at the Toronto meeting of the American Association for Thoracic Surgery.

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REFERENCES

1. Gage, I. M.: Personal communications.
2. Halsted, W. S.: The Employment of Fine Silk in Preference to Catgut and the Adoption of Transfixing Tissues and Vessels in Controlling Hemorrhage, *J. A. M. A.* 60: 1119, 1913.
3. Meade, William H., and Ochsner, Alton: Spool Cotton as a Suture Material, *J. A. M. A.* 113: 2230, 1939.
4. Meade, William H., and Ochsner, Alton: The Relative Value of Catgut, Silk, Linen, and Cotton as Suture Materials, *SURGERY* 7: 485, 1940.
5. Meade, William H., and Long, Carroll H.: Cotton as a Suture Material, *J. A. M. A.* 117: 2140, 1941.
6. Miller, H. E., and Prejean, O.: A Comparative Analysis of Total, Supravaginal, and Vaginal Hysterectomies, *Am. J. Obst. & Gynec.* 42: 380, 1941.
7. Ochsner, Alton, and DeBakey, Michael: Therapeutic Considerations of Thrombophlebitis and Phlebo Thrombosis, *New England J. Med.* 225: 201-227, 1941.

the region of the celiac axis. The upper limit of the tumor could not be felt at the cardia. Therefore the lateral ligament of the left lobe of the liver was divided and the lobe displaced toward the right exposing the esophageal hiatus of the diaphragm. The peritoneum was incised and the esophagus isolated and surrounded with a tape. The esophagus was found to be involved in a continuous mass with the stomach. The tumor extended up the wall of the esophagus into the posterior mediastinum for a distance of about 5 cm. Above this, smooth and soft pliable esophageal wall could be palpated but not visualized. The entire tumor mass was movable everywhere except possibly in the region of the gastric vessels posteriorly.

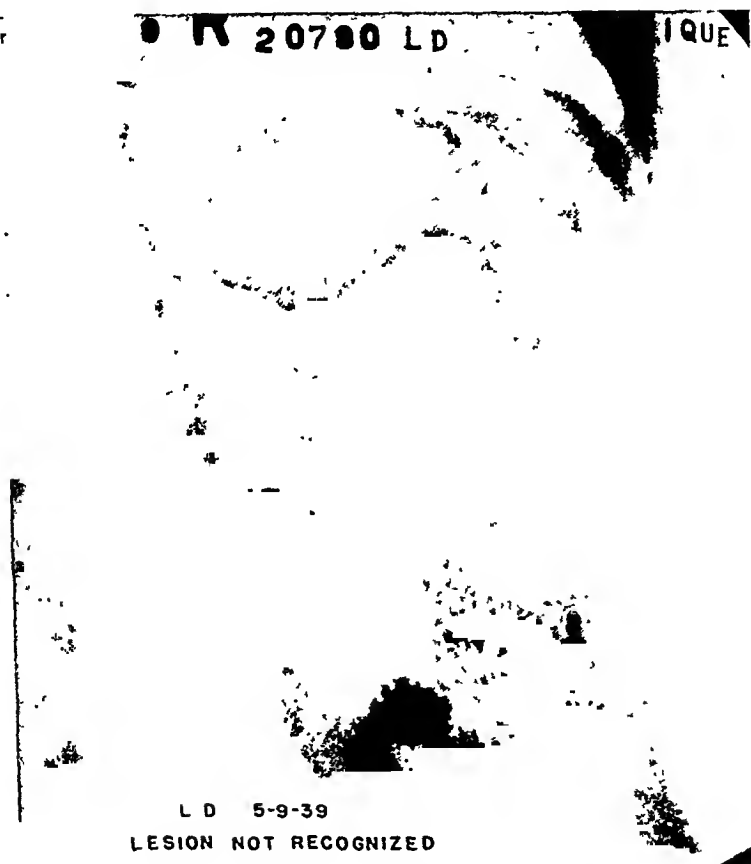


Fig 1.—X-ray taken in May, 1939, at which time carcinoma of the stomach was not recognized

There were no palpable metastases in the pelvic shelf and no palpable liver metastases. Several lymph nodes along the greater curvature were enlarged and several were removed for pathologic examination. It was realized that radical removal of the entire tumor mass was possible only by performing a total gastrectomy with a combined laparotomy and transthoracic resection of the lower esophagus with splitting of the diaphragm and then intrathoracic esophagojejunostomy. This procedure is of such magnitude that it did not seem wise to attempt it at this time without special preparation of the patient and full consent of the family. Therefore nothing

Association for Thoracic Surgery. His patient, unfortunately, did not survive the operation.*

CASE REPORT

L.D., a 52-year-old Swedish woman, was admitted by me to the Lenox Hill Hospital on Sept. 28, 1940. She had a history of two and one-half years of pain in the gastric region. Two years before admission she had gone to a doctor. X-rays were taken and reported negative (Fig. 1), but it was suggested that they be repeated. Powders and diet gave relief. There followed a several months' period of remission of symptoms. The patient did not return to the doctor. Ten months before admission the symptoms returned and this time were not relieved by treatment. Nausea and vomiting were present. There was marked loss of appetite and loss of forty pounds in weight since the onset of the disease.

The past history and family history were irrelevant. The patient was married and had three children.

Physical Examination.—Head and neck were negative. Heart and lungs were negative. In the abdomen there was some fullness in the epigastrium but no definite tumor was palpable. Weight, 130 pounds; pulse, 68; blood pressure 108/65.

Laboratory Findings.—Gastric analysis following a test meal showed absence of free hydrochloric acid and a low total acidity of 10. Lactic acid and blood were absent. Wassermann was negative. Blood count, Hb., 92 per cent; red blood cells, 4,750,000; white blood cells, 11,600; polymorphonuclear leucocytes, 64 per cent; lymphocytes, 33 per cent; monocytes, 1 per cent; eosinophiles, 2 per cent.

X-ray Examination.—Following a barium meal no obstruction or deformity of the esophagus was seen at fluoroscopy. A flat, filling defect measuring approximately 7 cm. in length was seen in the region of the midgreater curvature extending to the posterior wall of the stomach. This portion of the stomach seemed markedly stiffened and did not transmit peristaltic waves. Slight irregularity of the upper greater curvature was noted, which may possibly represent further extension toward the fundus. The prepyloric region and duodenum appeared normal (Fig. 2). At six hours the stomach was empty except for traces of barium. The deformity in the middle third of the stomach had the characteristic roentgen appearance of a malignant neoplasm.

Permission was given by the patient and the family for an exploratory operation and it was understood that a total gastrectomy might be necessary. A transfusion of whole blood of 500 c.c. was given two days before the exploratory operation.

First Operation.—On Oct. 2, 1940, under general anesthesia, a left paramedial incision was made. A tremendous tumor of the stomach was found involving the middle third and entire fundus of the stomach. The gastrohepatic omentum was split and exploration showed a firm hard infiltration around the gastric vessels in

*The operation performed for a similar lesion was done April 2, 1911. It was an extensive carcinoma involving the lower third of the esophagus extending 2½ cm. above the diaphragm, the body of the stomach. The entire procedure was performed by the approach with resection of the tenth rib, with the tips of the pancreas and spleen, and the portion of the esophagus involved in the tumor. An intrathoracic esophagojejunostomy was performed with the edema of the esophagus and the cutting through of the sutures. The anastomosis was not completely satisfactory for this reason. An enteroenterostomy was performed just below the opening in the transverse mesocolon where the loop of the jejunum was brought up. A leaf of omentum was brought up to cover the jejunum and the region of the anastomosis, and the diaphragm was reapproximated in two layers around it. Airtight drainage was placed into the pleural cavity. The patient stood the operation well but then ran a course of continued sepsis with high fever and died on the ninth postoperative day. A post-mortem examination was obtained but limited to the region of the operation. There was evidence of a defect along the suture line of the anastomosis with resulting empyema and a localized abscess under the diaphragm extending from the surgical hiatus of the diaphragm posteriorly to involve the end of the pancreas and the duodenal stump. The enteroenterostomy was water tight and the suture line of the duodenal stump was intact.

the region of the celiac axis. The upper limit of the tumor could not be felt at the cardia. Therefore the lateral ligament of the left lobe of the liver was divided and the lobe displaced toward the right exposing the esophageal hiatus of the diaphragm. The peritoneum was incised and the esophagus isolated and surrounded with a tape. The esophagus was found to be involved in a continuous mass with the stomach. The tumor extended up the wall of the esophagus into the posterior mediastinum for a distance of about 5 cm. Above this, smooth and soft pliable esophageal wall could be palpated but not visualized. The entire tumor mass was movable everywhere except possibly in the region of the gastric vessels posteriorly.



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There were no palpable metastases in the pelvic shelf and no palpable liver metastases. Several lymph nodes along the greater curvature were enlarged and several were removed for pathologic examination. It was realized that radical removal of the entire tumor mass was possible only by performing a total gastrectomy with a combined laparotomy and transthoracic resection of the lower esophagus with splitting of the diaphragm and then intrathoracic esophagojejunostomy. This procedure is of such magnitude that it did not seem wise to attempt it at this time without special preparation of the patient and full consent of the family. Therefore nothing

further was done and the abdomen was closed in layers. The patient made an uneventful recovery. Pathologic examination of the removed lymph nodes showed only hyperplasia.



FIG. 2.—X-ray taken before operation showing extensive involvement by carcinoma.

Interim Course.—With the full knowledge of the extent of the lesion an esophagoscopy was performed by Oberrender on the twenty-sixth postoperative day. The findings were as follows: 36 cm. from the upper jaw the esophagus was constricted and the mucosa was thickened but not irregular. This occurs in a concentric fashion and gives the impression of being a periesophageal infiltration with no signs whatever of neoplasm within the lumen. Biopsy was taken from the posterior wall where the thickening of the mucosa was most marked. Pathologic examination of this specimen showed edematous esophageal mucosa with no sign of malignancy. X ray

examination made at this time showed no constriction or deformity of the esophagus except little, if any, dilatation of the esophagus above a slight constriction at the lower end (Fig. 3). The patient was discharged from the hospital, Nov. 4, 1940, the thirty-third postoperative day, for a short period of home convalescence and preparation for the second operation. Consent for this procedure as outlined above was given by the family. Weight on discharge was 120 pounds.

While at home the patient was on a high protein and caloric diet with accessory vitamins, especially cevitamic acid and vitamin B complex. After twelve days she was readmitted to the hospital with a gain in weight of two pounds.



Fig. 3—X-ray of lower end of esophagus taken after the first operation with knowledge of presence of carcinoma of lower end of esophagus. Narrowing of lumen of esophagus is shown.

Preoperative preparation was as follows: (1) High protein diet; (2) cevitamic acid and vitamin B complex; (3) daily intravenous infusions of 1,500 c.c. of 5 per cent glucose in saline solution for three days before operation; (4) blood transfusion of 400 c.c. of blood two days before operation; (5) sulfanilamide gr. 15 every four hours for three days before operation; (6) collection of 2,000 c.c. of citrated blood the day before operation.

Clinical Findings Before Second Operation.—Two days before operation the blood count was as follows: Hemoglobin, 12 Gm. or 83 per cent; red blood cells, 3,850,000; white blood cells, 10,800; polymorphonuclear leucocytes, .65 per cent; lymphocytes, .30 per cent; monocytes, .2 per cent; eosinophiles, .3 per cent. Red cell volume, 44 per cent; blood plasma specific gravity, 1.0256; blood plasma protein, 6.36 per cent; blood plasma chloride, 616 mg./100 mil. Total base, 150 meq. per liter.

Second Operation (Nov. 22, 1940).—Basal avertin with inhalation anesthesia was used. Intravenous infusion was started before operation by placing a cannula into the vein of the left arm as all the superficial veins were so small and invisible that this was the only feasible method. A Levin tube was placed into the stomach to keep this empty.

The scar of the previous laparotomy just to the left of the midline was excised. The abdomen was opened and recent adhesions between the abdominal wall, omentum, stomach, and left lobe of the liver were freed. The gastrocolic omentum was divided from the pylorus along the greater curvature to the gastrosplenic ligament and along the fundus. The gastrohepatic omentum was then divided from the pylorus to the region of the gastric artery. The duodenum was divided with the aid of the dePetz clamp, the stump buried with silk sutures, and the head of the pancreas stitched over the suture line. The stomach was then easily collapsed by suction on the indwelling Levine tube and the further freeing of the stomach continued. The stomach was adherent to the under surface of the diaphragm in the region of the esophageal hiatus where the peritoneum had been incised at the time of the first operation. These adhesions were severed between ligatures with some difficulty. The greatest difficulty was to free the stomach posteriorly in the region of the gastric artery. This division was finally accomplished, freeing the entire stomach up to the esophagus at the diaphragm. The esophagus was then freed at the hiatus as far as the finger could reach. A laparotomy pad was wrapped around the stomach and tied with tape. Hereupon a loop of jejunum was taken about eighteen inches from the duodenojejunal juncture and brought upwards toward the diaphragm antecolically. At the lower end of these two limbs an enteroenterostomy was performed. One black silk thread was placed as a marker near the dome of the afferent loop and two black silk threads as markers near the dome of the efferent loop. This entire loop was then temporarily tied to the laparotomy pad surrounding the stomach. The abdominal wound was then closed using through-and-through steel alloy wire for the peritoneum, rectus muscle, and rectus sheath. Several fine interrupted chromic sutures were placed between these steel alloy wires for exact approximation. The skin was closed with interrupted silk sutures and the wound dressed with gauze and adhesive.

Citrated blood was started at this time through the cannula in the brachial vein. The patient was then placed on her right side. An intercostal incision was made along the seventh interspace, a small section of the seventh, sixth, and fifth ribs being resected near the vertebral column. The intercostal tissues were ligated and divided and the pleural cavity entered along the seventh intercostal space and the incision lengthened upward posteriorly. The rib spreader was inserted. Adhesions between the lung, parietal pleura, and upper surface of the diaphragm were transilluminated and then divided, freeing the lung, the upper surface of the diaphragm, and the mediastinum. The pleura over the mediastinum was incised exposing the esophagus all the way down to the diaphragmatic hiatus. The upper end of the tumor was felt about 5 cm. above the diaphragm. The phrenic nerve was crushed, paralyzing the diaphragm. The latter was then incised from the central tendon to the hiatus, making it very easy to draw up the stomach, with jejunal loop attached, into the thoracic cavity. It was at once disappointing to note that the mesentery

of the jejunal loop was not long enough to bring this up into the chest as easily as had been anticipated. The Levin tube was then withdrawn out of the stomach into the esophagus just above the level of the tumor. Continuous suction was applied to the tube to keep the esophagus empty. The entire mediastinum and lower chest cavity was protected with gauze pads moistened in one-half per cent lysol solution in order to try to prevent gross soiling of these areas. The efferent loop, marked with two black silk threads, was then sutured to the posterior surface of the esophagus at a point above the upper limit of the tumor. There was a good deal of tension and in order to relieve this the jejunum was temporarily sutured to the cut edge of the diaphragm. After the esophagus had been fastened thus to the jejunum posteriorly the esophagus was divided above the tumor and the specimen composed of the entire stomach and lower 5 cm. of the esophagus was removed in one piece (Fig. 4A and B). Hereupon an incision was made into the jejunum just distal

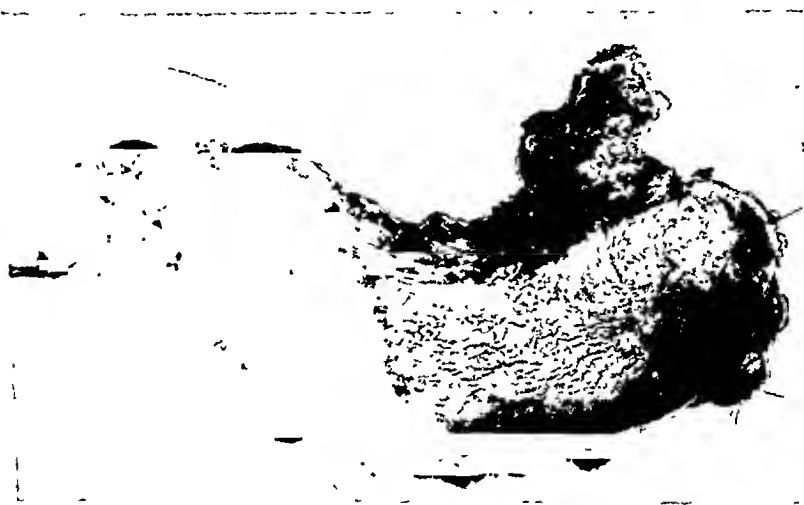


Fig. 4A.—Photograph of specimen of stomach including the lower 5 cm. of the esophagus.

to the dome of the jejunal loop. The Levin tube which had been drawn into the esophagus was then pushed down again and into the efferent loop of the jejunum for as long a distance as possible. There was some difficulty in doing this and it could not be pushed down as far as had been hoped. Esophagojejunostomy was then completed. It was necessary to place interrupted mattress silk sutures to successfully close the anterior suture line because straight sutures easily cut through the friable esophagus due to the unfortunate tension. After the anterior suture was placed, the afferent loop of the jejunum was brought over across the suture line in a manner similar to the technique proposed by Roseoe Graham in the intra-abdominal esophagojejunostomy in total gastrectomy. It was not possible to do this in an ideal manner but a covering had to be improvised and the parietal mediastinal pleura was also used to cover and reinforce the anastomosis. The jejunum which had temporarily been sutured to the cut surface of the diaphragm to relieve tension during the performance of the anastomosis was then separated and re-sutured in the proper position close to the esophageal hiatus in the diaphragm. The diaphragm was then sutured from the central tendon toward the jejunum at the hiatus. The esophagojejunostomy then looked quite satisfactory although there was definitely more tension than had been anticipated. Intercostal airtight drainage

was instituted two interspaces below the incision and the drainage tube placed fairly close to the region of the anastomosis. The chest was closed in the usual manner using chromic catgut around the ribs, continuous fine chromic catgut for the intercostal muscles and for the muscles, giving airtight closure. The lung was expanded during this procedure. The skin was closed with interrupted silk sutures and compression dressing applied.



Fig. 4B.—Photograph of specimen opened showing the thickened walls of the esophagus and stomach containing the carcinoma.

The patient's general condition was satisfactory at the end of the operation. The pulse was of fair quality, the rate 120, and the blood pressure satisfactory.*

Postoperative Course.—The patient was placed immediately into an oxygen tent and the blood transfusion continued through the cannula. Following the transfusion 5 per cent glucose in saline solution was substituted alternating each 1,000 c.c. between saline solution and distilled water. The patient was stimulated alternately with metrazol and caffeine sodium benzoate. During the first day there was 400 c.c. of pleural drainage. On the second day 500 c.c. of citrated blood was given through the intravenous cannula. Some water was allowed to flow by gravity through the indwelling Levin tube; this worked well. On the third day 10 per cent glucose in saline solution was allowed to drip through the Levin tube at the rate of 125 c.c. per hour. The infusion was continued. Blood hematocrit on this day was normal, as were the chlorides and serum protein. The infusion was discontinued, therefore, after having run continuously for three days. Albumin water was added through the Levin tube and on the fourth day ice pills were allowed by mouth. One third milk and lime water with cevitic acid was given through the tube. On the fifth

*I am indebted to Dr. Herbert C. Mahr for his assistance during this operation.

day one-half ounce of water was given every hour by mouth. On the following day there was intestinal content drainage around the pleural drainage tube with profuse drainage through the tube itself. Methylene blue and milk swallowed by mouth did not appear through the drainage tube at this time. With this leakage of intestinal content fluid balance was maintained easily through the Levin tube. Temperature varied between 99.6° and 101.6° F. since the operation. There was no evidence of spreading mediastinitis. Bedside x-ray examination showed the lung well expanded. On the tenth day both wounds were dressed. They were clean and healed by primary union and all sutures were removed. The pleural drainage tube was changed and a transfusion of 500 c.c. of whole blood given. On the nineteenth day x-ray examination with barium swallowed showed that most of it ran into the jejunum. On the twenty-first day the intestinal fistula was closed and all feedings were given by mouth. On the twenty-second day the chest drainage tube was shortened and on the twenty-fourth day the Levin tube was withdrawn easily and the patient

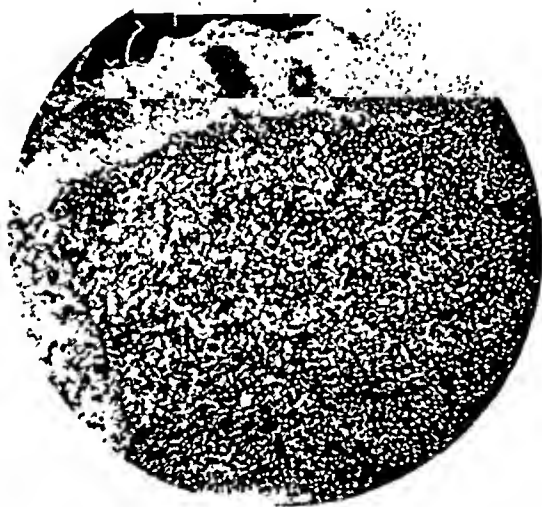


Fig. 5.—Low-power microphotograph showing involvement of submucosa of esophagus by carcinoma.

allowed out of bed. The fistula had lasted nineteen days. On the thirty-second day the chest tube was withdrawn and two days later the patient was receiving 2,100 calories per day by mouth with additional vitamins in liver extract. The patient's weight had dropped to a low of 102 pounds (Fig. 6.1 and B).

Postoperative Clinical Findings.—Blood examinations six weeks after operation. On Jan. 4, 1941, the hemoglobin was 9.6 Gm. or 63 per cent; red blood cells, 3,030,000; white blood cells, 10,700; polymorphonuclears, 73 per cent (28); lymphocytes, 26 per cent; monocytes, 1 per cent. Blood urea nitrogen, 7.2 mg. per 100 c.c.; creatinine, 0.5 mg.; uric acid, 2.4 mg.; sugar, 76 mg.; CO₂ combining power, 51.9 per cent. Hematocrit, 38; plasma specific gravity, 1.0244; plasma protein, 5.54; plasma albumin, 3.34; plasma globulin, 2.20; plasma chlorides, 549; serum diastase, 76. One month later, Feb. 7, 1941, the values of blood examinations were: 12.2 Gm. hemoglobin; red blood cells, 4,050,000; white blood cells, 9,200; polymorphonuclear leucocytes, 72 per cent (24); lymphocytes, 24 per cent; monocytes, 2 per cent; eosinophiles,

2 per cent. Hematocrit, 45; blood plasma, specific gravity 1.0247; plasma protein, 6.05; plasma CO_2 combining power, 68.3; plasma chlorides, 546; total base, 145.0, and serum diastase, 41. Stool examination, Jan. 4, 1941, revealed many yeast cells, some digested and undigested muscle fibers, some vegetable remains, occasional white blood cells, occasional fat globules, and bacteria.

Pathologic Examination.—The specimen received fresh was a stomach complete with 5 cm. of the esophagus attached. The stomach measured 17 cm. in length, 7 cm. in width, and 3.5 cm. in thickness. The serosal surface was tan-pink, smooth and glistening throughout. The wall over the entire stomach including the first 2 to 3 cm. of the esophagus was markedly thickened and firm. This thickened, firm area ended about 4 cm. from the duodenum. The rugae were markedly elevated. The mucosal surface was mottled, tan-pink to purple in color. On section, the wall throughout the thickened area was gray-pink, firm, smooth, and glistening.



Fig. 6.—A, Photograph of patient after operation showing healed laparotomy wound
B, Photograph of patient showing healed thoricotomy wound.

Microscopic examination of sections taken through the thickened area revealed a tumor arising in the mucosa of the stomach. It replaced the mucosa in a small area, but infiltrated the wall of the stomach throughout. The tumor cells were small or medium sized with a scanty cytoplasm and fairly large, vesicular or hypochromatic nuclei. Mitotic figures were inconspicuous. These cells formed no regular structures, being seen often singly or in groups, though occasionally they formed small nests and cords which infiltrated between the muscle fibers. They were supported and accompanied by a rather abundant connective tissue stroma which was quite cellular and markedly infiltrated with round cells. The growth invaded all the

layers of the stomach wall and extended beneath the intact mucosa into the esophagus to within 5 mm. from the edge of the specimen (Fig. 5). The pyloric end of the stomach was free of tumor tissue. The diagnosis was carcinoma of the stomach (linitis plastica).

Final Postoperative Course.—The remainder of the patient's course was a gradual decline. The esophagojejunostomy anastomosis was easily dilated several times with an olive bougie. Swallowing was satisfactory for the remainder of the patient's life (Fig. 7). The appetite steadily declined and carcinoma cachexia set in. Shortly before the death of the patient a jejunostomy was performed (March 30,



Fig. 7—X-ray showing functioning of anastomosis four months after operation. Note level of diaphragm and loop of jejunum above level of diaphragm within thoracic cavity. Loop is somewhat dilated to take the place of the stomach. Wire staples in the duodenal stump and steel alloy wires in the abdominal wall are also to be seen.

1941) for feeding purposes. At the time of this operation it was seen that the patient had a generalized carcinomatosis involving the liver, parietal and visceral peritoneum, intestinal mesentery and omentum. X-ray examination of the chest showed evidence of pulmonary metastases. The patient died on April 14, 1941, approximately five months after the major operative procedure. Unfortunately, an autopsy could not be obtained.

COMMENT

Total gastrectomy with removal of the lower esophagus and an intrathoracic esophagojejunostomy is feasible. This, I think, is best performed by means of a laparotomy and immediately following thoracotomy. Experience in this case shows that it is better to bring the loop of the jejunum up into the thorax retrocolically instead of antecolically. Examination on cadavers at the autopsy table since this experience, has shown that the entire root of the mesentery slides upward through the retrocolic opening in the transverse mesocolon for a small distance and therefore allows the jejunum to be brought up higher into the chest with resulting lessened tension on the suture line at the site of the anastomosis. The enteroenterostomy which is, of course, essential should lie then just below the opening in the transverse mesocolon.

If difficulty is found in freeing the stomach in the region of the spleen Lahey has recently advised the removal of the spleen together with the stomach rather than spending time in trying to separate the stomach from the spleen.

A jejunostomy performed at the same time as the laparotomy (Clute and Bell) is definitely better than the indwelling Levin tube passing through the site of anastomosis. This tube at the site of the anastomosis probably tends more to the development of a fistula with leakage. In a recent successful total gastrectomy, we have employed a jejunostomy for feeding purposes with great satisfaction. It adds very little time to the procedure, being accomplished in a few minutes. It has been a question in my mind whether the intestinal fistula in this case originated from an area of necrosis or damage to the intestinal wall at the point where the jejunum had been sutured temporarily to the edge of the diaphragm. On the other hand, it is more likely that it came from the site of the esophagojejunostomy anastomosis. However, it was noteworthy that methylene blue solution and milk did not immediately appear from the fistula opening but the drainage was mostly intestinal in character. At any rate the fistula lasted nineteen days and then closed spontaneously.

The preoperative preparation of these patients is of vital importance in all cases of major, upper abdominal surgery. High protein diet and high vitamin intake are essential. Vitamins A and D are important for healing of epithelial structures. Vitamin B complex is important for the proper functioning of the gastrointestinal tract and vitamin C is important for the intercellular cement and the prevention of edema at the site of the anastomosis.

The formula for jejunostomy feedings as suggested by Clute and Bell is very valuable and we have been using it to advantage. It is as follows: peptonized skimmed milk, 500 c.c.; one egg, well-beaten; haliver oil

and viosterol, 3 minims; syrup of vitamin B complex, 15 c.c.; cevitamic acid, 300 mg.; thiamine chloride, 6 mg.

Blood transfusion before operation and the use of citrated blood or blood plasma during the operation are most valuable adjuvants.

Sulfanilamide or sulfadiazene before operation helps to prevent infection below the diaphragm and within the pleural cavity and mediastinum. Recently, in a case of total gastrectomy I used 4 Gm. of sulfanilamide powder under the diaphragm at the site of the anastomosis. In the future I will use sulfanilamide powder in the posterior mediastinum and pleural cavity in place of the lysol wipes employed in this case.

An oxygen tent postoperatively is a great help for the patient. It maintains a high oxygen concentration and keeps the patient in a steady cool temperature which relieves breathing a great deal.

SUMMARY

1. A successful case of total resection of the stomach with the lower 5 cm. of the esophagus is reported. It was followed by an intrathoracic esophagojejunostomy.

2. Preoperative preparation, operative technique, and postoperative care are discussed. These factors are most important for success in such major procedures.

3. It is hoped that the report of this case, though fatal five months after the operation due to generalized carcinomatosis, may encourage other surgeons to attempt similar operations. The experience of others will help to improve the technical procedure. Only by experience, and its report in literature, can better results be obtained.

REFERENCES

1. Uhlhorn, E. J.: Totale Exstirpationen des Magens, *Arch. f. klin. Chir.* 144: 593-611, 1927.
2. Finney, J. M. T., and Rienhoff, W. F.: Gastrectomy, *Arch. Surg.* 18: 140-162, 1929.
3. Allen, A.: Total Gastrectomy for Cancer of Stomach, *Am. J. Surg.* 40: 35-41, 1938.
4. Peck, G. T., and Livingston, E. M.: Gastric Carcinoma—General Technique, *Am. J. Surg.* 45: 165-218, 1929.
5. Clute, H. M., and Albright, H. L.: In *Treatment of Cancer and Allied Diseases*, Peck and Livingston, editors, vol. 2, New York, 1940, Hoeber, 997-1007.
6. Graham, Roscoe: A Technique for Total Gastrectomy, *SURGERY* 8: 257-264, 1940.
7. Clute, H. M., and Bell: Jejunostomy for Postoperative Feeding, *Ann. Surg.* 114: 462-471, 1941.
8. Waugh, J. M., and Giffen, L. A.: Total Gastrectomy and Partial Esophagectomy for Carcinoma, *Proc. Staff Meet., Mayo Clin.* 16: 363-365, 1941.
9. Linhey, P.: Splenectomy With Total Gastrectomy, *Surg., Gynec. & Obst.* 73: 341-344, 1941.
10. Garlock, John H.: The Problem of Carcinoma of the Cardiac End of the Stomach, *Surg., Gynec. & Obst.* 73: 244-256, 1941.
11. Churchill, Edward D.: Personal Communication, December, 1941.

AN OPERATION FOR INGUINAL HERNIA BASED UPON THE UTILIZATION OF COOPER'S LIGAMENT*

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THE numerous modifications of the classic Bassini operation for inguinal hernia imply clearly that the original operation has not proved entirely satisfactory. The sole justification for an addition to the long list lies in the belief that the proposed operation offers direct support, as well as some measure of reduction, of the undefended space. The Bassini operation and its variations all lay down a shelf which is intended to resist permanently a hernial protrusion. Whether the conjoined tendon or rectus sheath or aponeurosis of the external oblique are joined to the reflected surface of Poupart's ligament, with or without re-enforcement by other tissues (fascial sheets or sutures), the objective remains a protective shelf and not a direct support of the undefended space. The latter may be partially reduced by closure of the gap in the transversalis fascia. Essentially, however, complete reliance against the recurrence of a hernial protrusion is placed on the barrier of a shelf which is not directly applied to the undefended space. The following operative procedure offers direct support to the mesial portion of the undefended space in the form of a slinglike buttress, and also reduces to some degree the size of that space. Cooper's ligament is utilized for the purpose, Poupart's ligament being relied upon for support in the conventional manner.

Technique: The cutaneous incision is placed somewhat nearer the inguinal fold than usual and the external oblique is split lower than usual in order to fashion a generous flap of the aponeurosis. A broader flap of external oblique than usual is required, for its approximation to the deeply situated Cooper's ligament is the essential part of the operation. After the isolation of the structures of the inguinal canal and the customary ablation of the sac (in the case of indirect inguinal hernia), the direct bulge or hernia is depressed with a suitable instrument. If there is serviceable transversalis fascia for the purpose, a purse-string suture is passed and tied for the inversion of the direct hernia. The essential step is the utilization of Cooper's ligament. The latter is exposed close to the spine of the pubis by following the reflected (deep) surface of Poupart's ligament into the pelvis. A thin but definite fibrous

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membrane medial to the iliac vein and apparently continuous with Poupart's ligament is traversed, the blunt dissector used for the purpose following the curve of the pelvis. The glistening free surface of Cooper's ligament, closely applied to the pubic ramus, is visualized by the placement of a narrow (one-quarter inch) malleable (ribbon) retractor. The external iliac vein is sufficiently isolated for its gentle lateral retraction with a second ribbon retractor, and Cooper's ligament is thereby fully exposed.

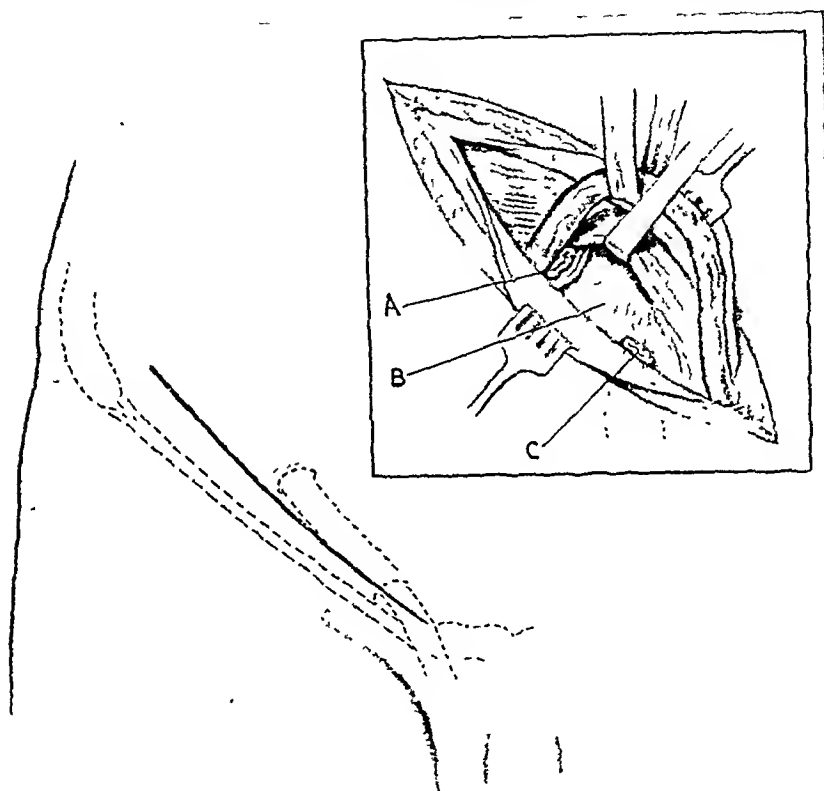


Fig. 1—Showing that the inguinal incision is lower than usual. In the insert are indicated (A) the stump of an ablated indirect *sic*, and (B) the protrusion of a direct hernia. If operation for femoral hernia is performed through an inguinal incision, the situation of the stump of an ablated femoral *sic* is indicated (C).

Two (or three) sutures, closely hugging the periosteum, are now passed through Cooper's ligament. I have found that the use of the Reverdin needle facilitates the passage of these deep sutures. In any event, attention should be called to the fact that the sutures are not correctly placed unless they are closely applied to the bone. After the passage of the sutures, which may be attended with some difficulty because of depth, the two ribbon retractors are removed. The mobilized aponeurosis of the external oblique is now drawn downward with two forceps and the

two (or three) sutures are passed through it at appropriate sites. The approximation should be tested before the sutures are tied. When tied, the external oblique should be drawn without undue tension downward and into the pelvis in the form of a sling. This curved support extending into the pelvis snugly supports and reduces appreciably the undefended space medial to the iliac vessels. If the sutures have been placed correctly, a pronounced curvature of the external oblique aponeurosis should be evident, and no dead space should remain. Poupart's ligament is now utilized. Its reflected surface lateral to the sling is approximated

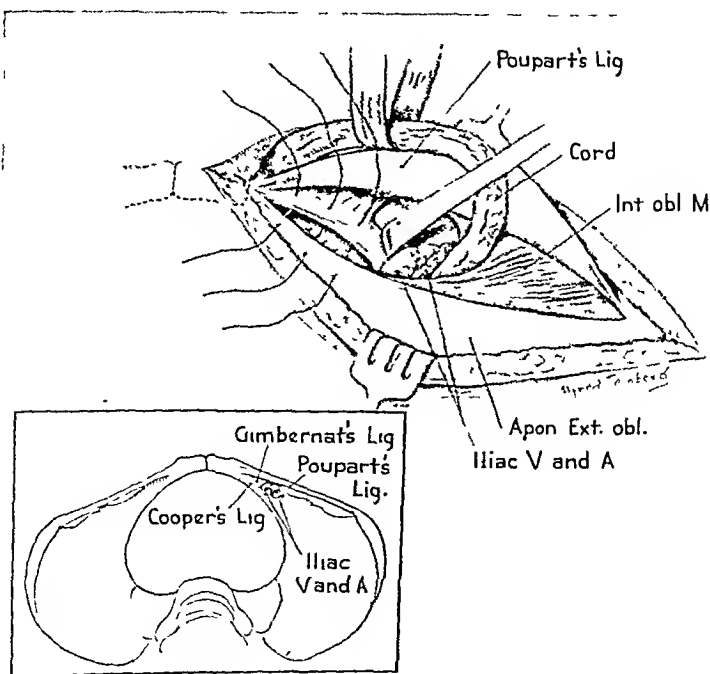


Fig. 2.—Sutures are passed between the aponeurosis of the external oblique and Cooper's ligament. Some of the fibers of Gimbernat's ligament may be included with advantage. The iliac vessels are not isolated as shown in the drawing.

to the external oblique in the customary manner. The medial portion of the reflected surface is then approximated by a few sutures to the surface of the external oblique over the sling in order to provide additional support. Silk technique is advocated.

The foregoing operative procedure has been employed for about three years. At first applied only to selected cases of direct inguinal hernia, it is now utilized for all direct hernias as well as for indirect hernias in which a direct component exists. There appears to be no reason to omit the procedure whenever the requirement is a direct support of the medial portion of the undefended space.

There have been no accidents referable to the operative procedure and none need be anticipated with careful technique. All structures in the field should be clearly visualized with special reference to the iliac vein. The sole danger of operation is damage to the vein, an accident which is obviated by gentle lateral retraction of that structure.

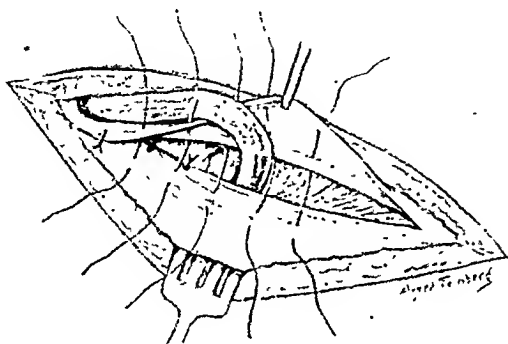


Fig. 3.—The sutures through Cooper's ligament have been tied and the reflected surface of Poupart's ligament is approximated to the adjacent aponeurosis of the external oblique. The structures of the cord can be displaced laterally to a greater extent than illustrated in the drawing.

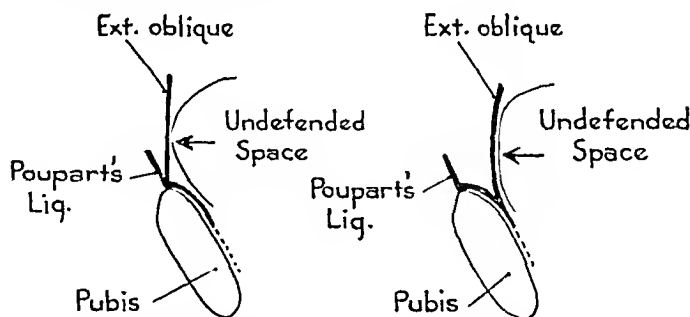


Fig. 1.—Vertical sections to illustrate the difference in effect between the Bassini type of operation and that described in the text. Left: The external oblique is attached to the reflected surface of Poupart's ligament and the undefended space is not directly supported. Right: The external oblique is attached to Cooper's ligament, Poupart's ligament not being utilized in the first layer. The undefended space is directly buttressed.

As compared with the usual operative exposure for hernioplasty, the field will appear surprisingly deep the first few times the described operation is performed. As a matter of fact, the depth always is great when the operation is performed for direct hernia in a stout individual. An unusually deep situation of Cooper's ligament comprises the only difficulty in the operation. As has already been stated, the passage of the suture through Cooper's ligament is facilitated by the use of the

Reverdin needle. Ordinary needles of small size can, however, be employed satisfactorily if their passage is not hurried. It is sometimes more convenient to pass the sutures through Cooper's ligament from the opposite side of the wound (side of the first assistant). If the sutures have been correctly placed, the aponeurosis of the external oblique can be approximated to Cooper's ligament without undue tension. After the sutures are tied, the result must be a firm, incurved, slinglike buttress and not a shelf. Of course, the utilization of the reflected (deep) surface of Poupart's ligament as an overlap offers additional firm support but this should be regarded as rather incidental insofar as the mesial portion of the wound is concerned. The utilization of Poupart's ligament as the essential structure for support begins immediately lateral to the sutures passed through Cooper's ligament.

The fact that uniformly good results in cases of direct and direct-indirect hernia have followed the described operation has little significance because the number of cases is too small and the time elapsed since the operation has been practiced is too short. The procedure is advocated at this time because it appears to offer a more definitive assurance of cure of direct and direct-indirect hernia than is afforded by the conventional procedures.

A RECONSTRUCTION OPERATION FOR LARGE MIDLINE INCISIONAL HERNIA

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THERE are several satisfactory methods for the repair of midline incisional hernia. It is for the extremely large, neglected hernia with wide separation of the anterior abdominal wall that we wish to describe this technique.

The Deformity.—(Fig. 1.) The hernial sac, by its mushroom shape, frequently gives the impression of a much larger opening than is actually found at operation. Since most pelvic operations are carried out through a right paramedian incision, the left rectus muscle is usually found to be completely inclosed in a normal sheath. The right rectus muscle frequently gives a similar impression, but actually the fascia of the anterior sheath is apt to be found retracted some distance from the hernial margin. The peritoneum, in providing the lining for the hernial cavity, is firmly adherent to the medial border of the muscle and the fascia of the anterior sheath by rather dense scar tissue simulating, in many instances, true fascia. Except, then, for the fact that there is an actual break in the continuity of the muscular and fascial structures of the abdominal wall in the midline, and that a hernial sac is present, we have a mechanical problem here differing not greatly from that of diastasis recti in this portion of the abdominal wall.

The method of reconstruction, here described, is an adaptation of that originally used and later described by us¹ for the repair of diastasis of the rectus muscles. This principle has been used in a fairly large series of cases over the past several years with almost uniformly good results. Beef fascia, it will be noted, is used for the muscular support instead of fascia lata. Clinically, beef fascia has been found to be perfectly satisfactory for this purpose, and it has been used by us over a period of fifteen years.

TECHNIQUE OF OPERATION

The Dissection.—(Figs. 2 and 3.) A large midline incision is made and the hernial sac is freely exposed. The sac is opened in its mid-portion. The lateral walls are dissected free from the overlying skin and fat. The dissection is carried laterally thoroughly to expose the

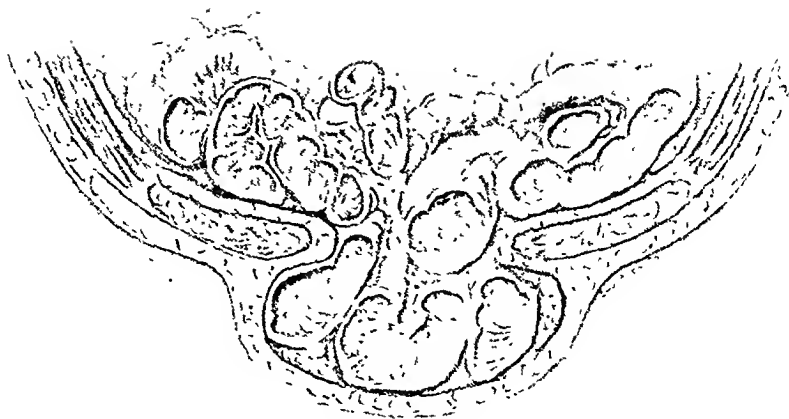


Fig. 1.—Cross section through hernia. Note the separation of the rectus muscles. The circular muscles are shortened.

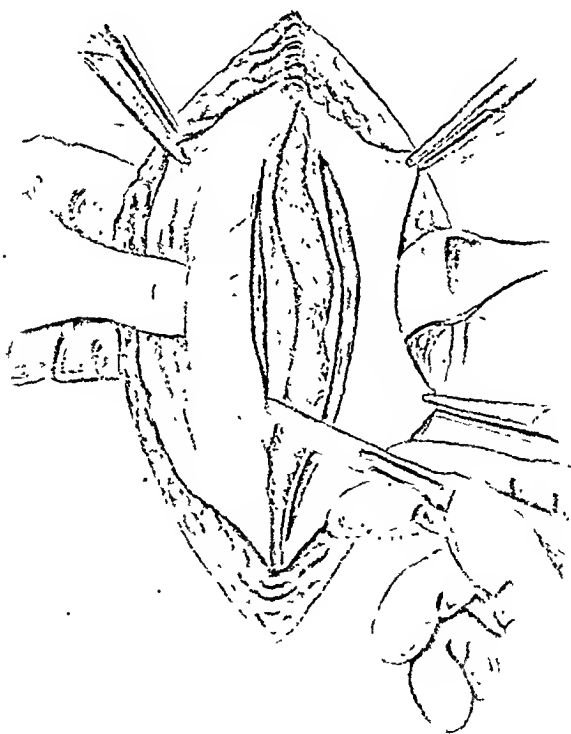


Fig. 2.—The sac has been incised and directed free. The anterior sheath of the rectus has been exposed. The posterior sheath of the left rectus has been opened. The posterior sheath of the right rectus is now being incised.

ventral surface of the anterior sheath on the right side, carrying the dissection to a point just beyond the lateral border of the sheath. This procedure is repeated on the left side. The excess sac is cut away leaving a border of about three-fourths inch around the margin of the



Fig 3—Cross section through hernia. The dissection has been completed on the left side. The right side has not been attacked.

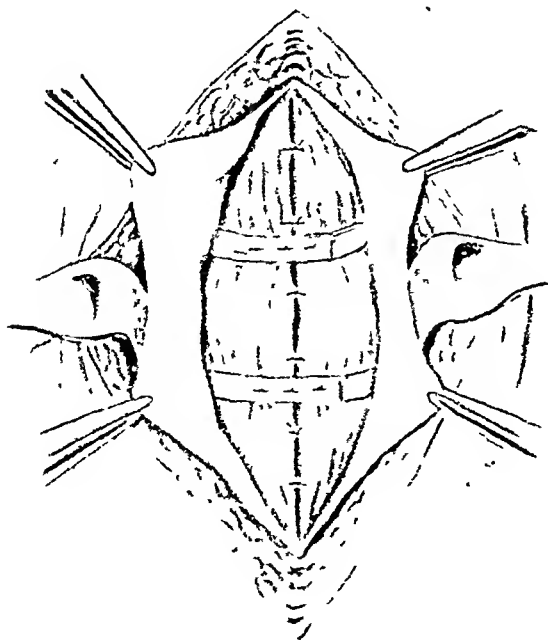


Fig 4—The posterior sheath has been closed. The rectus muscles have been dissected free and approximated in the midline with interrupted sutures and loops of beef fascia.

hernial opening. The anterior sheath of the rectus is not opened on either side as in most operations for ventral hernia. Rather, the posterior sheath is incised with the scalpel about one-half inch lateral to the hernial margin. The purpose of this posterior incision is to facilitate later closure as experience has taught that the posterior sheath can be approximated with much greater ease than the anterior sheath, and it is important in the dissection to save all the anterior sheath possible for later overlapping. This portion of the dissection can be more accurately accomplished if a grooved director is used.

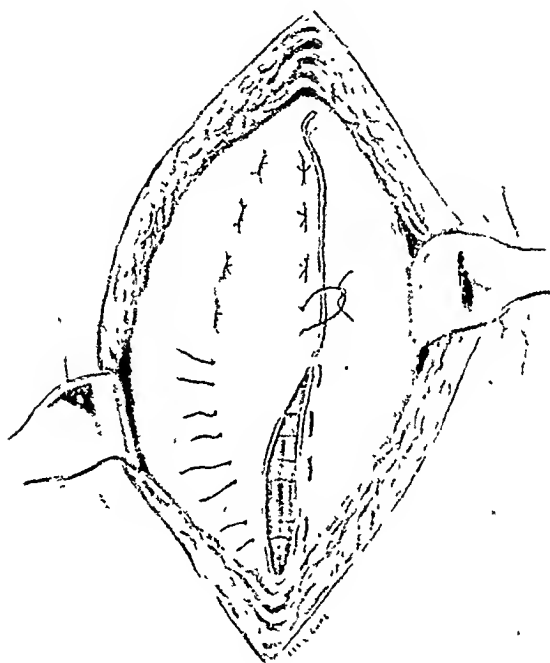


Fig. 5.—The anterior sheath of the rectus muscle is overlapped.

The rectus muscle on either side is gently dissected free of its bed, both anteriorly and posteriorly, care being taken to preserve its nerve and blood supplies.

Reconstruction of the Wall.—The peritoneum and as much of the attached fascia of the posterior sheath as is available are approximated in the midline, overlapping, if possible, using mattress or continuous sutures of No. 0 chromic catgut. After a thorough dissection this layer can usually be approximated without great difficulty.

The diastasis of the rectus muscles is then dealt with, the muscles being approximated at the midline and held in this position by two or

three loops of beef fascia which completely surround both museles, but without tension (Fig. 4).

The ends of these faseia loops are overlapped and fixed by interrupted sutures of No. 0 chromic catgut. The margins of the rectus museles are then approximated with interrupted sutures of No. 0 chromic catgut. The loops of beef fascia relieve the tension on these museles which, of course, are extremely friable and prevent these stitches from cutting loose.

The anterior sheath of the rectus musele is then overlapped, using mattress sutures of No. 1 ehromic eatgut (Fig. 5).

To summarize, we now have (Fig. 6) the peritoneum and the posterior sheath reapproximated. The two reetus museles are approximated to each other in the midline by interrupted sutures of No. 0 chromic eatgut reinforced to prevent lateral separation by loops of beef faseia. The anterior sheath of each rectus musele is approximated to its fellow of the opposite side and overlapped in the midline.

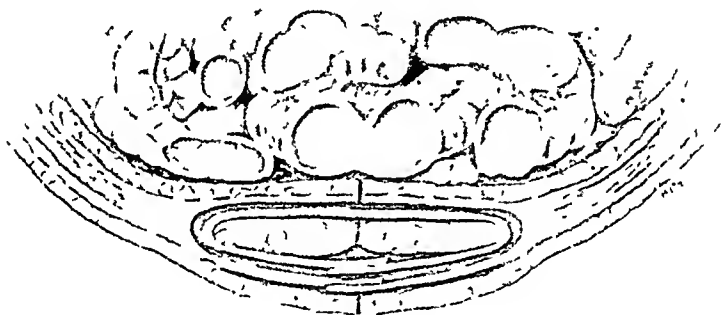


Fig. 6—Cross section through reconstructed wall at the level of a beef fascia loop. Note posterior sheath approximated, rectus musele approximated and surrounded by loop of beef faseia, and anterior faseia overlapped in the midline.

But, as frequently happens, regardless of how parsimonious the surgeon has been in his dissection, the faseia of the anterior sheath cannot be made to approximate completely in the midline (Fig. 7A). In this event, a portion of the approximated rectus musele does not have an anterior faseial covering. Beef faseia is then sutured in a zigzag fashion back and forth in a basket arrangement to reinforce the faseial element of the abdominal wall at this point. The beef fuseia is fixed to the anterior sheath by interrupted sutures of No. 0 chromic catgut.

Skin Closure.—(Fig. 7B.) The excess skin and fat are removed, and the wound is closed in the midline in the usual fashion. It must be borne in mind, however, that a large area has been undermined beneath the subcutaneous fat, and in spite of hemostasis some postopera-

tive oozing is to be expected. This will prove extremely troublesome in the healing of the wound unless adequate drainage is provided. Various methods of drainage have been tried by us, and it has been found that the most satisfactory results have followed the use of two transversely placed latex drains. One is introduced through a stab wound situated at the right of the superior angle of the wound and the other to the left of the inferior angle of the wound. The tubes are gradually withdrawn, a small amount each day, until the serous drainage has ceased. A snug abdominal binder is applied and worn during the hospital stay.

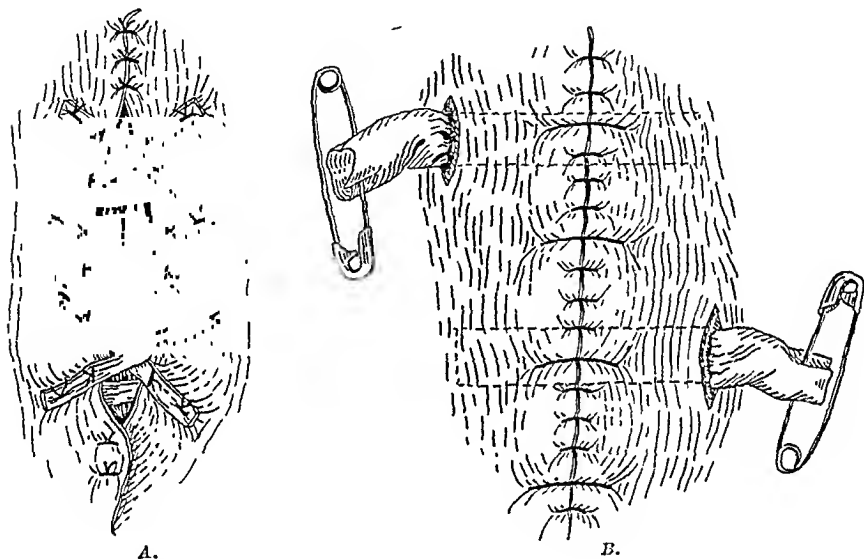


Fig. 7.—A. Method of reinforcing edges of the anterior aponeurosis with strips of beef fascia. Fascia lata might be used instead. B. Skin wound closed. Two transverse latex drains introduced through stab wounds.

Postoperatively, an abdominal belt should be worn from six to eight weeks. Beyond this period very little is to be gained from its use and it is felt that active exercise to the muscles should be encouraged.

REFERENCE

1. Rush, Leslie V., and Rush, H. Lowry: A Reconstruction Operation for Diastasis Recti, *SURGERY* 3: 200-202, 1938.

SIMPLIFIED METHOD FOR FORMATION OF AN ARTIFICIAL VAGINA BY SPLIT SKIN GRAFT

REPORT OF A CASE

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CONGENITAL absence of the vagina is associated usually with a nonfunctional uterus. For this reason, symptoms of retained secretion, often observed in acquired vaginal atresia, are seldom seen in these cases. A person with complete absence of the vagina, who has only rudimentary internal organs, may be otherwise fully developed, with manifestations of secondary sex characteristics and normal external genitals. These women may have normal sexual instincts, and in many instances are quite attractive. To deny these unfortunate individuals the opportunity for the pursuit of normal activities because of the absence of an organ the construction of which would be a comparatively simple surgical procedure, is to subject them unnecessarily to an abnormal social life. Certainly, with the procedure now improved and simplified, and with its associated low mortality, there is every justification for surgical construction of a vagina in those cases of congenital absence which are otherwise normal.

It is commonly believed that congenital absence of the vagina is rare, but this anomaly is probably more common than general observation might indicate, because some women with this condition never present themselves for treatment and many others are probably unrecognized. Flynn and Duckett¹ estimated that fully 500 cases of surgical correction for this abnormality have been reported in the literature. Engstad,² who has operated on nine such patients, estimates from his own experience that this congenital deformity occurs once in every five thousand cases. Counseller³ reports that the operation was performed sixteen times at the Mayo Clinic within a period of two years. Word⁴ has seen three cases within fourteen months. Frank⁵ reports that in twelve years he has seen more than thirty cases. In contrast, Newell,⁶ who is affiliated with an institution which admits thousands of women, has had only four patients in twenty-five years. At Charity Hospital in New Orleans, over a thirty-four-year period, this condition was found only six times in 502,081 female admissions, 123,676 of which were obstetric and gynecologic patients.

The variety of procedures for constructing an artificial vagina appearing in the literature is suggestive of the diversity of opinion which exists concerning the best operative technique. Roughly, this condition may be corrected surgically in one of three ways: by intestinal segment transplant, either utilizing the small intestine (Baldwin⁷) or the rectum (Schubert⁸); by pedicle transplant (Heppner⁹); or by free skin graft (Abbe¹⁰). Recently, Frank⁵ advocated a means of forming an artificial vagina without operation. This he does by gradually forcing inward the mucous membrane in the introital region without an incision. He has treated six patients in this way with one failure. However, one must question whether these results were obtained in cases where there was not a complete absence of the vagina but where there was a small rudimentary canal.

According to Dannreuther,¹¹ Paunz,¹² and others, Dupuytren attempted to establish a vaginal canal as early as 1817, by making an opening between the bladder and rectum into which a tampon was inserted. Since then various attempts have been made to improve the technique of construction, although the fundamental principle on which the operation is based has not changed.

In 1898, Abbe¹⁰ described a technique for construction of a vagina utilizing Thiersch grafts from the thigh applied over the surface of a rubber form, which in turn was inserted into the rectovesical space, which had been previously dissected out. The rubber form is removed in about ten days and contracture is prevented subsequently by plug bougies. This technique gave good results in one case. In a previous case Abbe had used the labia minora, but this was unsuccessful.

Baldwin⁷ was among the first to suggest intestinal transplantation for the formation of a vagina. In 1904, he conceived the idea for this operation, but was unable to try it out until 1907. Through an abdominal incision, a segment of the ileum was severed and carried down into the dissected tract prepared for the formation of the new vagina. The vagina, thus constructed, seemed normal in every way. Haberman¹³ improved Baldwin's technique by implanting a loop of small intestine. This method of intestinal transplantation is undesirable, particularly because of the high mortality rate. Monod and Iselin¹⁴ estimate a 21 per cent mortality following the operation. The intraperitoneal approach is probably largely responsible for this. Death in these cases has also been attributed to mesenteric thrombosis resulting from undue tension. Another disadvantage which the Baldwin technique incurs is the profuse mucous secretion following the procedure.

According to Schubert,¹⁵ Gersuny, in 1897, was the first to utilize a membrane cut from the rectum to line the vaginal canal. He first lined the perineum and sphincter ani with a strip of mucous membrane cut from the anterior wall of the ampulla without interrupting its connection with the rectum near the plica vesicorectalis. This was

sutured on the posterior wall of the bladder as far as the orifice of the urethra. Gersuny operated on three patients in this manner with satisfactory results, although it was necessary to wear a conical dilator to prevent narrowing. This, of course, is an objectionable feature.

Snegnireff,¹⁶ in 1904, divided the rectum in the sacral region, the lower end formed into a cul-de-sac, the upper end attached by suture to the skin, thus forming the artificial anus. The bridge between the anus and the vulva was divided and the wound closed so as to form a channel leading to the rectal segment. This method has been criticized because it forms a preternatural anus.

Schubert,¹⁵ in 1914, and Popow,¹⁷ in 1918, transplanted the lower rectum into the vulva, the upper rectal segment being utilized for re-establishing the continuity of the intestinal canal. The chief objection to this method is the comparatively high mortality rate (estimated at from 6 to 17 per cent). Monod and Iselin¹⁴ give a mortality of 8 per cent with Schubert's technique. Death is often the result of peritonitis. Other disadvantages of the method are the high incidence of fecal fistulas and rectal incontinence developing after this operation.

Graves,¹⁸ in 1917, revised the technique of flap transplant from the labia and thighs, which Heppner⁹ did in 1872. A transverse incision is made below the urethra and a canal between the bladder and rectum is made by blunt dissection. Each labium minus is dissected downward so that the entire mucous surface is utilized and the pedicle is large enough for good circulation. Two skin flaps are then taken from the medial aspect of the thigh and the four flaps are sutured together over a glass form. The form is removed and the mass is invaginated into the newly formed canal, where it is held in place by catgut sutures. The canal is then packed with tampons. The most undesirable feature of this operation is the fact that if the flaps necrose, there is no more tissue for a second attempt. It has, however, the advantage of an extraperitoneal approach.

Because of the grave risk involved in the Baldwin and Schubert operations, Frank and Geist¹⁹ devised a modification of the tube flap technique described by Gillies.²⁰ A tube pedicle skin flap is formed in the usual way. This is detached at its distal pedicle, split open, and wound around a hard rubber vaginal canal, which has been previously formed by blunt dissection. In 1932, they reported four cases in which this technique was followed, all of which resulted in successfully formed vaginas. Two outstanding disadvantages of this technique are the prolonged hospitalization (about ten weeks) and the defects over the inner aspect of the thigh at the site where the pedicle was formed. Among advocates of this method are Douglass,²¹ Davis and Cron,²² Grad,²³ and others.

In 1936, Monod and Iselin,¹⁴ after bluntly dissecting a space to conform to that of a normal vaginal cavity through a transverse incision

between the urethra and rectum, applied Thiersch grafts over a hard stent, which in turn was inserted into the cavity. They report one case with good results. In 1937, Burger²⁴ proposed lining the artificial cavity with fresh fetal membranes.

In 1938, McIndoe²⁵ suggested to Counseller³ an improvement in the skin graft technique to overcome contracture, which had been the reason for so many previous failures. A Thiersch graft removed from the thigh is wrapped around a mold and this, in turn, is introduced into the vaginal space which has been previously dissected out. The vaginal orifice is closed by approximating the labia minora over the mold, which is worn for a few weeks. Counseller³ reported sixteen operations in two years at the Mayo Clinic with excellent results in all but one case. This operation has given better results than any of the previously described procedures.

In 1938, Wharton²⁶ offered a simplified operative technique for constructing a vagina based on the principle that the vaginal epithelium has remarkable powers of proliferation. The operation consists of two steps: dissection of a space between the bladder and rectum, and the insertion of a vaginal mold covered by a condom. This mold is allowed to remain in place three weeks. He performed the operation in two patients and also reported two other cases which were treated in the same manner by Bureh and Hundley. The late results in two cases were entirely satisfactory; in the other two, only immediate results were known. However, he recommends this procedure not for cases of complete absence of the vagina, but for cases where a small rudimentary vagina is present.

In the light of the difficulty encountered in attempting to epithelize completely a newly formed vaginal cavity by means of a half thickness skin graft, it is not easy to understand the facility with which the entire cavity was epithelized solely by the proliferation of vaginal mucosa within the relatively short length of time stated. In our case approximately 85 per cent of the newly formed vaginal canal was lined by the half thickness skin graft applied at the first operation. A small finger-like projection of granulation tissue resulting from failure of some of the graft to take, extended from the border of the vaginal mucosa at the orifice backward into the vaginal vault. There was another defect at the dome of the reconstructed vaginal canal. No attempt was made to regraft these areas for fifteen weeks, in the hope that these small defects would epithelize. However, this did not occur and proliferation of epithelium took place here more slowly than in less contaminated areas. It was noted also that the proliferation of epithelium over the fingerlike projection of granulation was no more rapid than that in the deepest portion. Because of these observations and because of the behavior of proliferated epithelium elsewhere in the body, I see no reason for expecting epithelization of a reconstructed vaginal cavity

by proliferation of epithelium from vaginal mucosa during a time interval which is much shorter than that for the epithelization of an equal surface defect elsewhere.

It can readily be seen that the ideal technique has not yet been devised. The procedure of choice should be simple in performance, should involve as little danger of complications as possible, and should give satisfactory and permanent results. Whereas we are cognizant of the necessity of modifying the procedure to suit the individual case, the basic principles involved in the different procedures are conducive to analysis and evaluation. Reconstruction of the vagina by intestinal segment transplant is objectionable not only because of the high mortality but also because of the possible development of serious complications, such as peritonitis, thrombosis of the vessels in the mesenteric segment, perforation of the bladder and rectum, and extensive fulminating infections. The procedure which utilizes the surface of the labia majora as an included segment of mucosa requires more extensive dissection than some of the simpler procedures. Similarly, those methods which employ single pedicle or tube pedicle skin transplant not only require lengthy operative procedures with danger of possible infection but also necessitate extended periods of hospitalization. Another disadvantage is the unsightly scars on the inner surface of the thighs which must be subsequently repaired. The newly formed vaginal canal will probably be less satisfactory with the use of full thickness skin than with half thickness skin graft. The simpler methods which establish a vaginal canal by blunt dissection and effect proliferation of vaginal epithelization have already been discussed.

Therefore, the procedure which offers the best results with the least amount of operative maneuvers and minimal risk is the one which establishes the vaginal canal and affords a lining for it by the application of a half thickness skin graft. Among the factors which determine the successful take of skin grafts are an adequate blood supply, freedom from infection, and adequate and constant pressure. The first two factors are supposedly constant in many of these procedures. The last factor is greatly enhanced by the use of a vulcanite form of proper measurements, so carried as to distribute adequate and uniform pressure. We propose a modification of the skin graft transplant technique which is simple, safe, and satisfactory.

A transverse incision is made between the urethra and the anus at the point where the normal opening of the hymen is usually found in the virgin. Through this incision, with the index finger, a vaginal canal is dissected out bluntly between the rectum and the bladder extending upward to a normal depth. Extreme care is taken not to penetrate the peritoneal cavity. A half thickness skin graft is then removed from the inner surface of the thigh, provided this region is sufficiently hairless; otherwise, it is taken from the inner aspect of the arm. The skin

graft is then wrapped around a smooth vulcanite form, which has been made prior to operation, and the entire mass is inserted into the newly formed vaginal cavity. The piece of skin should be large enough to completely cover the form. The measurements of the cast (10 to 12 cm. long and 12 cm. in diameter) conform to those of a normal vaginal canal. It is cylindrical in shape and rounded at both ends, with a slight concavity on one side in the center and a proportionate convexity of the other. To the distal end (the portion which protrudes through the vaginal orifice) is attached a slight knob, not unlike the knoblike portion of a dumbbell. Through this knob are made two holes for the reception of rubber tubes, which are used to hold the vulcanite form firmly in place after it is inserted into the vaginal canal. These tubes exert the proper pressure for maintaining the form under suitable tension in a desirable fixed position. The two ends of the rubber tube are

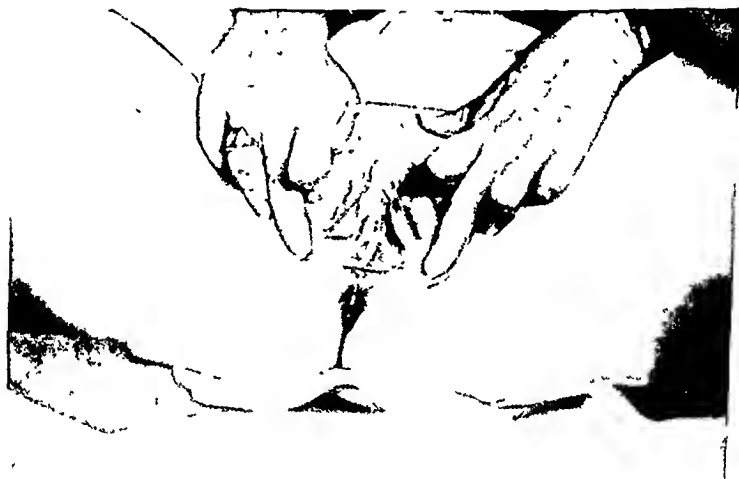


Fig. 1 --Photograph showing the normal anatomic appearance of the labia minora and majora as well as that of the clitoris. Note that there is no suggestion of a hymen or rudimentary vaginal canal. A firm diaphragm covered with mucosa is present. There is no dimpling.

attached to an abdominal belt anteriorly and posteriorly. The tube passes anteriorly downward through the opening in the mold between the thighs and then follows the gluteal fold to pass upward posteriorly. When the tubes are in place, they act as a perfect suspensory sling. These not only support the vulcanite form but hold it constantly in place by conveying elastic pressure through its contact with the form. The form, when worn, is nonirritating and is not uncomfortable to the patient. Because the vulcanite form has been made to conform to the size of the newly made vaginal canal, and because the pressure is properly applied by the rubber tubes acting as a sling support, the graft is held snugly in place in the vaginal canal and is kept in intimate contact

with the denuded surface of the canal as well as being maintained in a fixed immovable position. The patient is kept in bed in a prone position for approximately ten days, after which the form may be withdrawn, so that the newly lined vaginal canal may be cleansed and irrigated. The form not only maintains the desired size of the vagina, but it acts in intimate contact with the graft to support and constantly massage it, this latter action rendering the graft pliable and soft.

At the end of approximately two weeks, the graft has healed sufficiently to permit the patient to sit up in a chair with the form still in its fixed position. No discomfort whatever is experienced from the constant wearing of the vaginal cast. When strength permits, the patient



Fig. 2—Photograph showing the vaginal form inserted in the newly formed vaginal canal. Note the appearance of the rubber tubes where they pass through the openings in the knoblike portion of the distal end of the vaginal form.

resumes normal activity with the dilator constantly in place. Because of the ease with which the vulcanite form may be removed, daily douches may be taken and frequent inspection with cleansing of the canal may be made. The above routine insures normal expansion of the canal so that the desired pressure is constantly applied to the surface of the graft. Because of the action of the vulcanite form against the graft, the entire lining surface of the canal is constantly massaged, thereby rendering it pliable and soft. The form should be worn for about six months in order to avoid the possibility of contracture, which inevitably results if the surface is not constantly massaged for approximately that length of time.

The following case illustrates the technique described.

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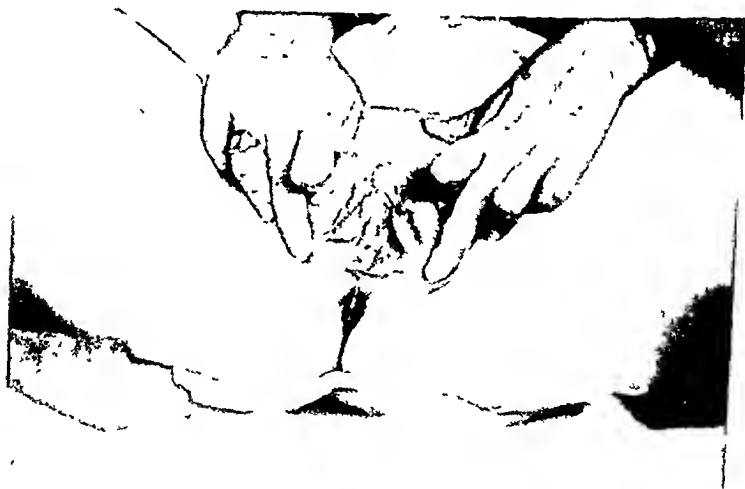


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The patient engaged in normal activities and was not aware of her abnormality until it was discovered when an examination of the perineum was made several years before. She had consulted surgeons at three clinics. At two of these the operation using the intestinal segment was advocated and at the other reconstruction by the creation of a vaginal cavity by blunt dissection and the insertion of a bougie was recommended. Because of the variation in the suggested technique and the prognosis, decision to have the operation performed was deferred for several years.

Physical examination revealed a healthy, attractive, white girl, 30 years old. Both breasts were normally developed. There were no tumors or abnormal growths. Female sex characteristics predominated. Examination of the vulva showed normal female distribution of pubic hair and the presence of the labia majora and minora. A surface of mucosa appearing as a flat normal indurated area lay between the labia minora. Complete absence of the vagina was indicated by the absence of indentation. Rectal examination disclosed a small tumorlike growth, which was probably a rudimentary uterus, and a resistance on palpation, which was apparently the left ovary. All other physical findings were normal. (See Fig. 1.)



Fig. 5.—Photograph showing the vaginal form compared with a large vaginal speculum.

On July 1, 1939, under cyclopropane anesthesia, after thorough cleansing of the vulva with normal saline solution and soap, an incision was made between the labia minora from the urethra downward to a point where the fourchette is normally found. An opening was made upward and backward in the region where the vagina is normally found, and by blunt dissection this was carried back 10 to 12 cm. To avoid perforating the rectum one finger of the assistant was placed in the rectum and a retention catheter inserted through the urethra into the bladder. Following this a form of the newly constructed vaginal vault was made from a plastic dental compound and over this was wrapped a split skin graft which had been removed from the medial surface of the left thigh. This was introduced into the newly formed vault where it was held fixed by means of through and through tension sutures inserted in the tissues at the orifice. A sterile pad was then applied and the legs held strapped for about twelve hours. Following the operation catheterization of the patient yielded a considerable quantity of urine, indicating that the bladder had not been perforated. Vaginal examination at operation revealed the absence of a uterus, but the presence of the adnexa.

REPORT OF CASE

This patient (Case No. M1535), a normal, white girl, aged 30 years, was admitted to a local hospital, July 1, 1939, with a diagnosis of congenital absence of the vagina.

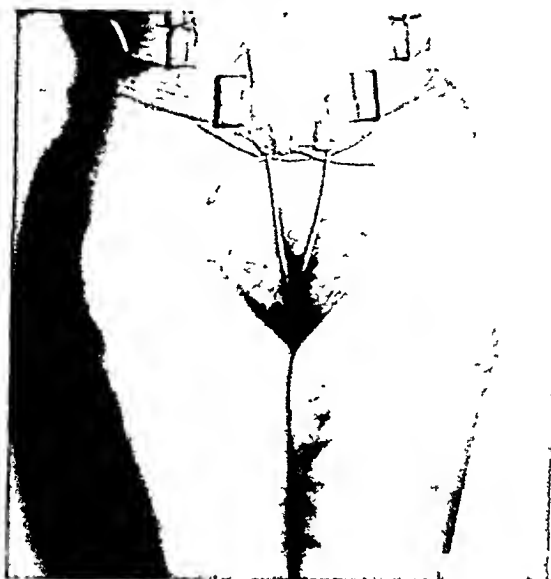


Fig. 3.—Photograph showing the attachment of the suspensory tubes to the lower medial border of the abdominal belt, anterior view.



Fig. 4.—Photograph showing the suspensory rubber tubes, posteriorly, as they course upward to follow the gluteal folds. From Figs. 3 and 4, one can see the support which is afforded the vaginal form by means of the suspensory tubing. An adequate amount of upward pressure is conveyed to the vaginal form thus assuring intimate contact of the form with the graft.

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The patient's postoperative course was uneventful, the temperature never exceeding 101° F. and becoming normal within a few days. The vulva was irrigated regularly. An 85 per cent take of the graft was obtained. The patient progressed nicely and was discharged, July 23.

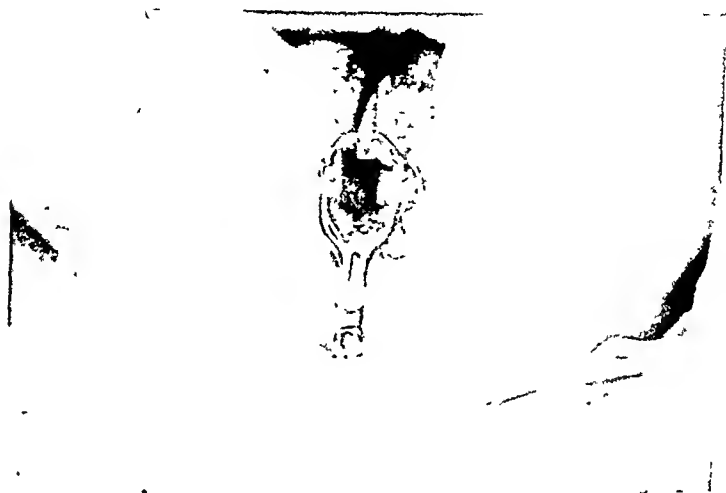


Fig. 6.—Photograph showing large vaginal speculum inserted into the newly constructed vaginal canal. Note the size of the canal after the speculum has been completely opened.



Fig. 7.—Photograph showing the normal appearance of the perineum following the construction of the vagina.

Due to the difficulty of retaining the form which had previously been made from a plastic dental compound, a vulcanite form was made to conform to the size of the newly made vaginal canal. A complete description of this form has already been given which enumerates the many advantages of this type of dilator over those which are commonly used. The patient was able to wear this form with comfort and because of the support afforded by means of the rubber tubes, a satisfactory

pressure was always applied. These tubes permit the form to be removed with ease and as a result of this frequent cleansing is permitted. The vulcanite mold is worn constantly during the first six months following operation. (See Figs. 2 to 5.)

Because of a slight area of granulation tissue at the orifice and another small area at the dome of the newly formed vaginal canal, on November 13, a second graft was removed from the left thigh and placed on the stent and the stent reinserted. A third graft was applied to a slight defect at the dome of the canal. Results following this procedure were satisfactory.

The patient was kept under constant observation for a period of six months, during which time she wore the vulcanite form continuously, changing it daily to permit cleansing and douches. At this time no tendency toward contracture was seen. The canal remained approximately the same size. The character of the skin graft which had been applied to establish a lining for the constructed canal showed definite change. In appearance the skin resembled mucous membrane. No microscopic section of this tissue was made since it has been shown by previous authors that skin grafts, when applied to defects in mucous membrane lined cavities, uniformly manifest a change which makes them not unlike mucous membrane in appearance. In some instances the microscopic picture shows a change which is similar to that seen in microscopic sections of mucous membrane.

Frequent examinations were made on this patient for two years and it was found that the character of the skin graft remained essentially the same as that described above and it showed no tendency to become unstable. No tendency to contracture occurred during this time. See Figs. 6 and 7.

SUMMARY

1. There is every justification for the construction of an artificial vagina in those cases of congenital absence which are otherwise normal.
2. Congenital absence of the vagina is not as rare as formerly assumed.
3. The various operative techniques for correction of this defect are reviewed briefly.
4. A modification of the skin graft transplant technique, which is simple, safe, and satisfactory, is proposed.
5. A case of congenital absence of the vagina in which this method was employed with excellent results is reported.

REFERENCES

1. Flynn, C. W., and Duckett, J. W.: Plastic Operations for Construction of an Artificial Vagina, *Surg., Gynec., & Obst.* 62: 753, 1936.
2. Engstad, J. E.: Artificial Vagina, *Journal-Lancet* 37: 329, 1917.
3. Comselle, V. S.: New Surgical Treatment for Congenital Absence and Traumatic Obliteration of the Vagina, *S. Clin. North America* 19: 1047, 1939.
4. Word, B.: Construction of Artificial Vagina, *South. M. J.* 33: 293, 1940.
5. Frank, R. T.: The Formation of an Artificial Vagina Without Operation, *Am. J. Obst. & Gynec.* 35: 1053, 1938.
6. Newell, Q. V.: Discussion in reference 3.
7. Baldwin, F.: The Formation of an Artificial Vagina by Intestinal Transplantation, *Ann. Surg.* 40: 398, 1904.
8. Schubert, G.: Anatomie and Topographic Considerations for My Operative Method in Vaginal Defect, *Zentralbl. f. Gynäk.* 47: 347, 1923.
9. Heppner: Cited by Paunz, reference 12.
10. Abbe, R.: New Method of Creating a Vagina in a Case of Congenital Absence, *Med. Rec., N. Y.* 51: 876, 1898.
11. Dannreuther, W. T.: Frank-Gleit Operation for Congenital Absence of Vagina, *Am. J. Obst. & Gynec.* 35: 452, 1938.

12. Pannz, A.: Formation of an Artificial Vagina to Remedy Congenital Defect, *Zentralbl. f. Gynäk.* 47: 883, 1923.
13. Haberland: Operation bei volligem Manzel der Scheide-vorschlag einer neuen operationsmethode, *Zentralbl. f. Gynäk.* 29: 263, 1907.
14. Monod, R., and Iselin, M.: Colpoplastie Pour Absence Congénitale de Vagin par un Procédé Amélioré de Greffes de Tierses Montées sur Tuteur Rigide, *Mém. Acad. de Chin.* 62: 997, 1936.
15. Schubert, G.: Concerning the Formation of a New Vagina in the Case of Congenital Malformation, *Surg., Gynec. & Obst.* 193: 376, 1914.
16. Sneguireff, W. F.: Zwei neue Fall von Restitutio vaginae per transplantationem ani et recti, *Zentralbl. f. Gynäk.* 28: 772, 1904.
17. Popow, D. D.: Cited by Meyer: Kolpoplastik, *Zentralbl. f. Gynäk.* 37: 639, 1918.
18. Graves, W. P.: *Gynecology*, Philadelphia, 1917, W. B. Saunders Company, pp. 385.
19. Frank, R. T., and Geist, S. H.: The Formation of an Artificial Vagina by a New Plastic Technie, *Am. J. Obst. & Gynec.* 14: 712, 1927.
20. Gillies, H. D.: *Plastic Surgery of the Face*, 1920, Oxford University Press.
21. Douglass, M.: Construction of Artificial Vagina, *Am. J. Obst. & Gynec.* 35: 675, 1938.
22. Davis, C. H., and Cron, R. S.: Congenital Absence of Vagina; Report of Two Cases Treated by Vaginal Plastic Operation, *Am. J. Obst. & Gynec.* 15: 196, 1928.
23. Grad, H.: Technique of Formation of Artificial Vagina, *Surg., Gynec. & Obst.* 54: 200, 1932.
24. Burger, K.: Künstliche Scheidenbildung mittels Eihäuten, *Zentralbl. f. Gynäk.* 61: 2437, 1937.
25. McIndoe, A. H., and Banister, J. B.: An Operation for the Cure of Congenital Absence of the Vagina, *J. Obst. & Gynaec. Brit. Emp.* 45: 490, 1938.
26. Wharton, L. R.: A Simple Method of Constructing a Vagina, *Ann. Surg.* 107: 842, 1938.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

CRUSH AND COMPRESSION INJURIES WITH UREMIC DEATH

JOHN MOHARDT, M.D., F.A.C.S., CHICAGO, ILL.

DURING the past year the British medical literature has contained reports of cases which, at first, were thought to be unique observations of this war. These were cases of crush and compression injuries accompanied by renal failure which for a time were considered to present a new syndrome. It is incredible, however, that this syndrome has not been associated with injuries sustained in civil practice (mine, automobile, and other types of accidents resulting in crush and compression injuries). It must be that the effects of such injuries were not observed carefully or not recorded, inasmuch as very little has appeared on the subject in the English literature. The studies of Bywaters and others⁵⁻⁷ have revealed references in German periodicals to cases occurring in the last great war.

During the Messinan earthquake, in Italy, a considerable number of persons were crushed, compressed, or buried. A German expedition arrived at the scene fourteen days after the catastrophe. Colmers,⁸ in 1909, described among eighty-three casualties from this earthquake nineteen victims suffering from acute fatal pressure necrosis, and in only one was there a history of oliguria with blood urine.

In 1916, Frankenthal¹⁴ described three soldiers who had been buried and who showed edema, bloody urine, and post-mortem isehemic muscle necrosis. However, no importance was placed on the findings in the urine. Other pathologists described similar material, some in journals now inaccessible. Among these Hackradt,²¹ in 1917, from Borst's laboratory described tissue from a patient who had been buried for nine hours, and in whom occurred edema of the legs and vesicles and bloody urine containing albumin and casts. The patient died on the fifth day. Necropsy showed muscle necrosis with associated tubular degeneration in the kidneys. Hackradt focused attention on the sharp distinction between acute hemorrhagic glomerulonephritis ("war nephritis") and the specific tubular degeneration in the kidneys associated with crush or compression injuries of the extremities and other parts of the body. He cites the autopsy findings of one case reported by Borst^{2, 3} and two cases by Bredauer.⁴ On the basis of autopsy findings, Hackradt points

12. Phunz, A.: Formation of an Artificial Vagina to Remedy Congenital Defect, *Zentralbl. f. Gynäk.* 47: 883, 1923.
13. Haberland: Operation bei volligem Manzel der Scheide-vorschlag einer neuen operationsmethode, *Zentralbl. f. Gynäk.* 29: 263, 1907.
14. Monod, R., and Iselin, M.: Colpoplastie Pour Absence Congénitale de Vagin par un Procédé Amélioré de Greffes de Tiersch Montées sur Tuteur Rigide, *Mém. Acad. de Chir.* 62: 997, 1936.
15. Schubert, G.: Concerning the Formation of a New Vagina in the Case of Congenital Malformation, *Surg., Gynec. & Obst.* 193: 376, 1914.
16. Sneguireff, W. F.: Zwei neue Fall von Restitutio vaginae per transplantationem uni et recti, *Zentralbl. f. Gynäk.* 28: 772, 1904.
17. Popow, D. D.: Cited by Meyer: Kolpoplastik, *Zentralbl. f. Gynäk.* 37: 639, 1918.
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accumulated products of metabolism into the injured muscles is the responsible agent. Frankenthal,¹⁴ Borst,^{2,3} and Schmincke⁴⁴ are of the opinion that the muscle necrosis is of local anemic origin based on the vasomotor paralysis of the vasomotor nerves, and that the bleeding into the tissues at the point of injury is diapedetic in origin.

Acute renal insufficiency is a common clinical finding in cases with crush or compression injuries, as has been recorded by Bywaters and Beall (1941);⁶ Beall, Bywaters, Belsey, and Miles¹ in 1941; and Mayon-White and Solandt,³⁰ also in 1941. The acute renal insufficiency is always accompanied by acute changes in the kidneys of a specific and unusual nature. The most definite changes found in the kidneys from the crush syndrome comprise the following: (a) light-brown casts resembling hemoglobin in secondary convoluted tubules; (b) proliferation of cells in some of these tubules; (c) the more intense focal lesions rupture the tubules and allow protrusions of albuminous material into venules; (d) large orange-brown casts are found in the medulla in many collecting tubules. Their presence is associated with damage and regeneration of the epithelium, and the casts are quite numerous. The essential pathologic lesion is restricted, then, to the ascending limbs of Henle's loops and the second convoluted tubules. The most severe of the tubular lesions implicates the walls of the small venules into which many of them have perforated.

It is difficult to find in the diseases of man any analogy for a condition of selective damage to the lower segments of the nephron, but evidence drawn from experimental lesions in animals may assist in elucidating the pathogenesis of a lesion of this kind. Dunn and Polson,¹³ in 1926, demonstrated that by introducing into the circulation of the rabbit large doses of uric acid in solution in the form of lithium monurate, selective damage could be produced in the ascending limbs of Henle, in the secondary convoluted tubules, and to some extent in the collecting tubules, while the first convoluted tubules remain normal in appearance. Necrosis of the epithelial linings is produced within an hour or so after injection, and the regenerative changes are in full swing by the fourth to the eighth day. In the regenerative phase the lesions show a distinct similarity to those seen in the kidneys of cases with crush or compression injuries. In these animals, just as in uranium or oxalate nephritis where the first convoluted tubules are selectively damaged, an anuria or oliguria is present with a rise in blood urea. These findings have been attributed by Dunn and Polson to nonselective reabsorption of filtrate through the damaged wall of the tubules into the venules thus escaping excretion. More recently, McFarlane (1941)²⁷ has shown that in the experimental nephritis of rats, which was described by MacKay and Oliver,²⁸ in 1935, and by Duguid,¹⁰ in 1936, the lesion is again restricted to the lower nephron segments, and he agrees with Dunn and Polson in attributing the special localization at this level to change of reaction in the filtrate.

out that such traumas, especially when they are multiple and involve the central nervous system, chest, abdomen, or pelvis, cause death as a result of widespread fatal embolism.

In microscopic studies of autopsy material the German authors found no disturbance in the circulation of the kidneys as evidenced by vascular engorgement. Brown corny cylinders were found in the tubules of the medullary substance and were considered to be the products of intense methemoglobin infarction in the pyramids. The marked reduction in the quantity of excreted urine was thought to be caused by blockage of the canaliculi with methemoglobin cylinders. Bredauer⁴ attributes the presence of free hemoglobin in the blood and the excretion of hemoglobin in the urine to the disintegration of muscle substance at the point of muscle necrosis, the formation of catabolic products there, and the absorption and circulation of the myohemoglobin and foreign proteins in the blood stream.

Minami,³⁷ in 1923, summarized the literature and investigated the material from three other cases from Piek's laboratory, cases which had been described by Lewin,²⁵ in 1919. Minami's description tallies exactly with the findings of Bywaters and Beall,^{5, 6} in 1941, in two victims buried by grenade explosion. On the second day following the event, these patients showed painful swelling of the thigh; on the fourth day, scanty bloody urine and tenderness in the kidney regions appeared; on the fifth day, only 100 c.c. of urine, less pigmented, was found; and on the sixth day, when death occurred, the urine was still scanty but not yellow, and contained red and hyaline casts. Necropsy showed grey muscle necrosis at the point of injury. The kidneys showed normal glomeruli, degeneration of the convoluted tubules, and pigmented masses and ribbons of debris in the collecting tubules and in Henle's loops. Minami pointed to the analogy between this condition and paralytic myohemoglobinuria of horses. He intended, were it possible for him to get fresh material, to identify the pigment spectroscopically. By the end of the last war the syndrome was well recognized by the Germans and was included in their textbooks of surgery. In Great Britain, however, it appears to have been unrecognized and undescribed prior to the present war. All such traumatic cases terminating in death should be investigated systematically, not perfunctorily.

In attempting to explain the peculiar muscle necrosis in compression injuries some interesting hypotheses have been advanced. Minami postulates that the muscle necrosis appears to result from indirect injury to the vessel walls without thrombus formation. As a result, a patchy, irregular distribution of the areas of necrosis occurs, not only in the lower extremities but in the muscles of the back, chest, abdomen, and buttocks, as well. Orth³⁸ explains the necrosis as a consequence of the indirect traumatic pressure. Wieting⁴⁶ believes that the necrosis is caused by a parenchymatous degeneration of the muscle elements. Groll¹⁹ thinks that colloid-chemical, osmotic, acid penetration of the

accumulated products of metabolism into the injured muscles is the responsible agent. Frankenthal,¹⁴ Borst,^{2, 3} and Schmincke⁴⁴ are of the opinion that the muscle necrosis is of local anemic origin based on the vasomotor paralysis of the vasomotor nerves, and that the bleeding into the tissues at the point of injury is diapedetic in origin.

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It is difficult to find in the diseases of man any analogy for a condition of selective damage to the lower segments of the nephron, but evidence drawn from experimental lesions in animals may assist in elucidating the pathogenesis of a lesion of this kind. Dunn and Polson,¹³ in 1926, demonstrated that by introducing into the circulation of the rabbit large doses of uric acid in solution in the form of lithium monurate, selective damage could be produced in the ascending limbs of Henle, in the secondary convoluted tubules, and to some extent in the collecting tubules, while the first convoluted tubules remain normal in appearance. Necrosis of the epithelial linings is produced within an hour or so after injection, and the regenerative changes are in full swing by the fourth to the eighth day. In the regenerative phase the lesions show a distinct similarity to those seen in the kidneys of cases with crush or compression injuries. In these animals, just as in uranium or oxalate nephritis where the first convoluted tubules are selectively damaged, an anuria or oliguria is present with a rise in blood urea. These findings have been attributed by Dunn and Polson to nonselective reabsorption of filtrate through the damaged wall of the tubules into the venules thus escaping excretion. More recently, McFarlane (1941)²⁷ has shown that in the experimental nephritis of rats, which was described by MacKay and Oliver,²⁸ in 1935, and by Duguid,¹⁰ in 1936, the lesion is again restricted to the lower nephron segments, and he agrees with Dunn and Polson in attributing the special localization at this level to change of reaction in the filtrate.

A feature which appears to be unique among the tubular changes in the reported cases is the localization of the most intense damage at points where the lower nephron segments lie in close proximity to veins. In uric-acid nephritis there seems to be little doubt that the lesion is determined by precipitation of the agent from a soluble form in which it is relatively harmless to a solid form which exerts the destructive effect. It seems possible that in the cases reported, also, a specific toxic substance is produced in the presence of acid, and that the proximity of venous blood has an influence in permitting a greater swing toward an acid reaction in this area than is reached at other parts of the nephron.

Nothing certain is known, as yet, of the nature or source of any toxic agent which may be responsible for the renal damage in cases of crush syndrome. The available facts, however, appear to justify the primary view to which most observers have adhered—that after release of the affected tissue from a compressed or more or less ischemic state, something toxic is absorbed from it into the circulation as the vessels reopen, and that the toxic agent affects the kidney in the course of excretion. The number and kinds of possible toxic agents which could so arise are conjectural and the suggestion that the cast material, which apparently contains myohemoglobin (Bywaters and Delory,⁷ 1941), is toxic is probably true. Uric and phosphoric acids have been suggested as possible toxic agents to the kidneys, since both of these molecules have a well-recognized origin in muscular tissue in the form of inosinic acid.

The part, if any, which may be played in the initiation of this syndrome by the lowered blood pressure in shock has yet to be determined. Bywaters and Beall,⁸ while recognizing that a fall of systemic pressure and dehydration may contribute toward the development of oliguria, could not attribute primary significance to these factors in their cases or those of others. There also appears to be general unanimity that the degree and kind of renal functional disturbance which develop after the crushing of limbs are quite distinct from any of the sequelae of ordinary surgical shock. The significance of selective involvement of the kidneys in the crush syndrome can hardly be overlooked.

In the records of fatal cases of crush injuries the brown casts in the renal tubules have been a conspicuous feature, and similar casts have been described in the urine of patients who recovered (Longland and Murray, 1941²⁶). The question has been raised as to whether blockage of tubules by these casts could be the cause of the renal disability, but histologic evidence on this point is inconclusive. The persistence of casts in the urine could easily depend on the diminution of the filtrate, whether this resulted from an impaired circulation, dehydration, or some other cause. The most important criticism of the blockage theory, however, has been made by Bywaters and Beall,⁸ who point out that if tubular obstruction alone were concerned, such urine as was secreted should theoretically be of normal composition, coming from unobstructed tubules, but in their experience the urine was little more than a glo-

merular filtrate with a urea concentrating factor of 1.6 to 3.8 in their Cases 1 and 2. This is confirmed by figures taken from Henderson's²² (1941) chart of a recovered case with a concentrating factor about 3.3 on the tenth day when the urinary output was about 700 c.c. In Cases 1 and 2, reported by Professor J. Shaw Dunn and others,¹¹ single observations on the eighth day gave concentration factors of only 2.7 and 3.3, respectively. Such extreme degrees of ablation of one of the highest functions of the kidney are of considerable moment and it is no doubt significant that among acute renal conditions the greatest reduction of concentrating power is known to occur when there is severe damage to tubular epithelium. This may be observed in mercurial nephritis in man and animals.

The clinical picture of fatal renal failure after crushing or compressing of limbs or other parts of the body, or after burns, is best presented by describing a typical case history: The patient has been buried for several hours with pressure on a limb or limbs. On admission to the hospital his condition may be good, the pulse and the blood pressure normal. There is swelling of the limb, some local anesthesia, and whealing. The edema spreads along the limb or limbs, movements of the limbs become limited or are absent, and various sensory disturbances may be present, such as anesthesia, hyperesthesia, or paresthesia.

In the crushed limb the changes observed include necrosis of the muscle of patchy distribution, hemorrhage into the muscle which may not be constant, edema of the limb, and an increased tension of the tissues within the fascial compartments of the limb. Intense arterial spasm appeared to be a common cause of the ischemia. Clinically, peripheral arterial pulsation was sometimes absent when the case was first seen. Loss of nerve function was recorded in the majority of the cases.

The hemoglobin is raised; a few hours later the blood pressure falls and shock ensues. This may be successfully combated by transfusions of serum, plasma, or blood. The urine, however, diminishes and contains albumin and many dark brown and black granular casts. The patient is alternately drowsy and anxious. Thirst and excessive vomiting are present commonly. The blood urea and potassium become progressively higher, the sodium chloride and the CO_2 combining power of the blood are progressively diminished, and death occurs in about a week.

Necropsy reveals necrosis of muscle and, in the renal tubules, degenerative changes and casts containing brown pigment. The casts, on microscopic examination, appear to be composed not of red cells but of desquamated epithelial cells, the pigment probably being due to hemoglobin excreted into the lumen from the blood stream. The gross and microscopic appearance of the kidney resembles the kidney of mismatched transfusion. There was, however, no clinical evidence of a transfusion reaction, and samples of plasma taken seventeen and forty hours after transfusions showed no increased color. Furthermore, fatal

cases with identical lesions in the kidneys are being reported, in which blood transfusion has not been given. Bywaters and Beall⁶ point out that the syndrome did not occur in any of twenty-five shocked and injured patients without severe muscle crush, treated in their hospital by blood or serum transfusion. The only common factor in all of the reported cases is muscle necrosis.

The prognosis depends upon many factors. The duration of the crush did not seem to bear much relation to survival. Those crushed for a long time might recover. Another factor influencing prognosis was the extent of the injury. Particular care should be exercised in a case of muscle damage by crush or compression, for at the beginning the serious cases can not be distinguished from the comparatively minor ones. A further factor was the rise in the blood urea. In the severe cases in which the patients recovered there was a fall in the blood urea at about the same time as death occurred in the fatal cases. The urea could rise to very high levels, and the patient might recover without any treatment whatever. Recovery occurred in about one-third of the patients admitted. In about two-thirds of the cases, death took place from renal failure, generally at about the fifth to the eighth day.

Treatment is directed toward dilution of the toxins and promotion of diuresis, while adrenal cortex extract is given to check the rise in blood potassium which results from the increased permeability of injured muscle, at the site of injury, and the more rapid escape of intercellular ions. Primary amputation of the affected limb has been tried in a few cases but has failed to save life, while in the others when recovery occurred, it did so without amputation. Decompression of the limb by multiple incisions into the limb was tried in a few cases without results. Patey and Robertson³⁹ thought the syndrome might be due not to liberated autolytic bodies from damaged muscles, but to a loss of substances from the circulation into the affected limb on the release of compression. This would readily explain the shock and possibly the renal failure as a secondary manifestation of shock. If this is true, large intravenous injections of plasma or serum would tend to increase the loss of blood constituents into the damaged limb in the same manner as in a burn, with subsequent increase in edema. The logical procedure seemed to be to prevent this leakage of fluid from the circulation. Patey and Robertson treated two cases by applying intermittent positive pressure up to 60 mm. of mercury to the edematous areas, using an especially large blood pressure cuff. In both cases there was a greatly increased output of urine immediately, softening and later disappearance of the edema, a fall of blood urea to normal, and recovery. On the basis of this finding, it would be logical to bandage the limb firmly by wide bandages immediately at the time the debris is removed from the limb. The limb should be elevated and splinted as soon as possible. For the associated peripheral spasm probably heat and intravenous atropine and papaverine are indicated.

It should be impressed on rescue workers that the real danger to people pinned down by wreckage is kidney failure, and therefore it is of paramount importance to ensure copious diuresis, particularly at the time they are about to be released from the pressure. The advantages of a good urinary flow would be a dilution of chemical substances in the kidney tubules and perhaps prevention of precipitation of myohemoglobin casts. As pointed out by Maitland,²⁹ in 1941, isotonic sodium sulfate solution has been advocated as a potent diuretic from time to time. In view of the original oliguria present, he suggests that isotonic sodium sulfate solution be given by the drip method, intravenously, up to several pints a day.

No severe additional damage or difficulty would accrue by the immediate application of a tourniquet above the compression. This should be maintained until good diuresis has started, then the tourniquet should be released gradually.

These patients have a low alkaline reserve and alkalization of the patient should be instituted as early as possible. The administration of alkalis in quantities adequate to render the urine alkaline is a rational procedure. Sodium bicarbonate and sodium citrate should be given by mouth from an early stage in quantities of 200 or 300 gr. a day. The use of a sodium salt must be emphasized because of the high blood potassium present which might conceivably be one of the biochemical factors leading to death. Improvement of urinary output occurs after extensive alkaline therapy. Good diuresis, of course, cannot be maintained in the presence of circulatory collapse. Hence, shock should be treated by transfusion, the transfusion fluid being serum or plasma.

CONCLUSIONS

1. The admission of a large number of casualties to a hospital may result in the early crush syndrome being overlooked unless examination is systematic. The patient may look well in the early stages and be passed over temporarily.

2. To date, the present war has produced no new surgical problems. However, one outstanding observation has been made—the appearance of grave and often fatal kidney damage after prolonged compression of the limbs.

3. Most authors agree that the essential pathologic lesion is muscle necrosis at the site of the injury; that the breakdown of autolytic products from dead or dying muscle is the main factor which damages the kidneys. Two main effects are produced in the kidneys: Some chemical substance is liberated which poisons the tubule selectively, and there is present, also, a tubular blockage factor, quite possibly resulting from the precipitation of myohemoglobin casts.

4. It is generally agreed that the crush syndrome is a definite entity and though resembling mismatched transfusion and the effects of prolonged shock, it is differentiated by its distinct clinical, biochemical, and pathologic features.

5. Primary amputation in the early stages has been tried in a few cases and has resulted fatally. Decompression of the limb by multiple incisions has also been tried in a few cases without result. Therapeutic attempts are directed toward the treatment of shock, dilution of the toxins and promotion of diuresis, restoration of a depleted alkaline reserve, compression by intermittent positive pressure or by firm bandaging of the injured limb, immobilization of the injured part and intravenous atropine and papaverine for release of the associated arterial spasm.

REFERENCES

1. Beall, D., Bywaters, E. G. L., Belsey, R. H. R., and Miles, J. A. R.: Case of Crush Injury With Renal Failure, *Brit. M. J.* 1: 432-434, 1941.
2. Borst, M.: Einwirkung der Schussverwundung und sonstiger Kriegsbeschädigungen auf die einzelnen Körpergewebe. In Borehard and Schmieden, Leipzig, 1917, J. A. Barth, chap. 2, pp. 61-100.
3. Borst, M.: Pathologisch-anatomische Erfahrungen über Kriegsverletzungen, Volkmanns Sammlung. klin. Vorträge, Leipzig, 1917, J. A. Barth, no. 735, 297-328.
4. Bredauer: Pathologische Befunde bei Verschüttungen im Kriege, Inaug.-Dissert., München, 1920.
5. Bywaters, E. G. L., and Beall, D.: Crush Injury With Impairment of Renal Function, *Brit. M. J.* 1: 29, 1941.
6. Bywaters, E. G. L., and Beall, D.: Crush Injuries With Impairment of Renal Function, *Brit. M. J.* 1: 427-432, 1941.
7. Bywaters, E. G. L., and Delory, G. E.: Myohaemoglobinuria, *Lancet* 2: 649, 1941.
8. Colmers: Ueber die durch das Erdbeben in Messina am 28. Dec. 1908 verursachten Verletzungen, *Arch. f. klin. Chir.* 90: 701-727, 1909.
9. Doerr, R.: Die Anaphylaxieforschung im Zeitraum von 1914-1921. *Ergebnisse d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap.* 5: 72-274, 1922.
10. Duguid, J. B.: Primary Lesion in Phosphate Nephritis, *J. Path. & Bact.* 43: 321-326, 1936.
11. Dunn, J. S., and others: Renal Lesions in Two Cases of Crush Syndrome, *Lancet* 2: 549, 1941.
12. Dunn, J. S., Haworth, A., and Jones, N. A.: Urea Retention in Experimental Oxalate Nephritis, *J. Path. & Bact.* 27: 377-400, 1924.
13. Dunn, J. S., and Polson, C. J.: Experimental Uric Acid Nephritis, *J. Path. & Bact.* 29: 337-352, 1926.
14. Frankenthal, L.: Ueber Verschüttungen, *Virchow's Arch. f. path. Anat.* 222: 332-345, 1916.
15. Frankenthal, L.: Die Folgen der Verletzungen durch Verschüttung, *Beitr. z. klin. Chir.* 109: 572-587, 1918.
16. Froehner: Lehrbuch der Pathologie und Therapie der Haustiere, Stuttgart 1: 353, 1904.
17. Further Cases of Crush Injury Collected by Medical Research Council Subcommittee on Traumatic Oedema, *Brit. M. J.* 1: 440-451, 1941.
18. Giese, E.: Experimentelle Untersuchung über Erfrierung, *Vierteljahrsschr. f. ger. Med.*, ser. 3, 22: 235-263, 1901.
19. Groll: Direkte Kriegserkrankungen durch gröbers physikalische Einwirkungen, *Schjernings Handbuch d. Aerztl. Erfahrungen im Weltkriege*, vol. 8, 1921.
20. Guenther, H.: Ueber den Muskelfarbstoff, *Virchow's Arch. f. path. Anat.* 230: 146-178, 1921.
21. Hackradt, Adolf: Ueber akute, todliche, vasomotorische Nephrosen nach Verschüttung. (München) 43 pp. 8°. Berlin, 1917, L. Schumacher.
22. Henderson, R. G.: Recovery From Uraemia Following Crush Injury, *Brit. M. J.* 2: 197, 1941.
23. Kitt: Lehrbuch der pathologischen Anatomie der Haustiere, Stuttgart, F. Enke 2: 423, 1911.
24. Krehl-Marchand: Handbuch der allgemeinen Pathologie, S. Hirzel, Leipzig, Bd. 1, 1908.

25. Lewin, Alfred: Zur pathologischen Anatomie der Verschüttungen. 46 pp. 8°. Berlin, E. Ebering, 1919.
26. Longland, C. J., and Murray, J.: Case of Recovery From Crush Syndrome, *Lancet* 2: 158, 1941.
27. McFarlane, D.: Experimental Phosphate Nephritis in Rat, *J. Path. & Bact.* 52: 17-24, 1941.
28. MacKay, E. M., and Oliver, J.: Renal Damage Following Ingestion of Diet Containing Excess of Inorganic Phosphate, *J. Exper. Med.* 61: 319-333, 1935.
29. Maitland, A. Ian L.: Case of Crush Injury With Recovery, *Lancet* 2: 446, 1941.
30. Mayon-White, R., and Solandt, O. M.: Case of Limb Compression Ending Fatally in Uraemia, *Brit. M. J.* 1: 434-435, 1941.
31. Meyer-Betz, F.: Beobachtungen an einem eigenartigen mit Muskellähmungen verbundenen Fall von Hämoglobinurie, *Deutsches Arch. f. klin. Med.* 101: 85-127, 1910-1911.
32. Meyer-Betz, F.: Ueber Hämoglobinurie beim Menschen und Pferde, *München. med. Wehnschr.* 58: 768, 1911.
33. Meyer-Betz, F.: Zur vergleichenden Pathologie der paroxysmalen Hämoglobinurie, *München. med. Wehnschr.* 58: 1737, 1911.
34. Miller, Hugh: Crush Injury and Experimental Uraemia, *Brit. M. J.* 685, 1941.
35. Miller, J. W.: Ueber elektive Hämoglobinfärbung, und den Ort der Hämoglobinausscheidung in der Niere, *Frankfurt. Ztschr. f. Path.* 11: 403-422, 1912.
36. Miller, J. W.: Ueber die Histologie der Niere bei Hämoglobinurie auf Grund elektiver Hämoglobinfärbung, *Centralbl. f. allg. Path. u. path. Anat.* 22: 1025-1035, 1911.
37. Minami, S.: Ueber Nierenveränderungen nach Verschüttung, *Virchow's Arch. f. path. Anat.* 245: 247-267, 1923.
38. Orth: Kasuistisches über Verletzungen durch Verschüttungen, *München. med. Wehnschr.* 58: 1406-1408, 1916.
39. Patey, D. H., and Robertson, J. D.: Compression Treatment of Crush Injuries of Limbs, *Lancet* 1: 780-782, 1941.
40. Pick, L.: Zur pathologischen Anatomie der Verschüttungen, *Aerzt. Sachvestaendigen Ztg.* 26: 13-16, 1920.
41. Reineboth: Experimentelle Untersuchungen über den Entstehungsmodus der Sugillationen der Pleura in Folge von Abkühlung. Zugleich ein Beitrag zu den pathol.-anatomischen Veränderungen nach starkerer Temperaturniedrigung, *Deutsches Arch. f. klin. Med.* 62: 63-88, 1898-1899.
42. Reineboth and Kohlhardt: Blutveränderungen in Folge von Abkühlung, *Deutsches Arch. f. klin. Med.* 65: 192-204, 1899-1900.
43. Ribbert, H.: Bemerkungen zu der Mitteilung von Miller über die Histologie der Niere bei Hämoglobinurie, *Centralbl. f. allg. Path. u. path. Anat.* 23: 62-63, 1912.
44. Schwineke: Die Kriegserkrankungen der quergestreiften Muskulatur, *Volkmanns Sammlung. Klin. Vorträge*, no. 758-759, 1918.
45. Volkmann, J.: Subnormale Temperaturen bei Verwundungen und Verschüttungen, *München. med. Wehnschr.* 64: 338-339, 1917.
46. Wieting: Ueber Wundliegen, Drucknekrose und Entlastung, *München. med. Wehnschr.* 65: 311-314, 1918.

5. Primary amputation in the early stages has been tried in a few cases and has resulted fatally. Decompression of the limb by multiple incisions has also been tried in a few cases without result. Therapeutic attempts are directed toward the treatment of shock, dilution of the toxins and promotion of diuresis, restoration of a depleted alkaline reserve, compression by intermittent positive pressure or by firm bandaging of the injured limb, immobilization of the injured part and intravenous atropine and papaverine for release of the associated arterial spasm.

REFERENCES

1. Beall, D., Bywaters, E. G. L., Belsey, R. H. R., and Miles, J. A. R.: Case of Crush Injury With Renal Failure, *Brit. M. J.* 1: 432-434, 1941.
2. Borst, M.: Einwirkung der Schussverwundung und sonstiger Kriegsbeschädigungen auf die einzelnen Körpergewebe. In Borchard and Schmieden, Leipzig, 1917, J. A. Barth, chap. 2, pp. 61-100.
3. Borst, M.: Pathologisch-anatomische Erfahrungen über Kriegsverletzungen, Volkmanns Sammlung. klin. Vorträge, Leipzig, 1917, J. A. Barth, no. 735, 297-328.
4. Bredauer: Pathologische Befunde bei Verschüttungen im Kriege, Inaug.-Dissert., München, 1920.
5. Bywaters, E. G. L., and Beall, D.: Crush Injury With Impairment of Renal Function, *Brit. M. J.* 1: 29, 1941.
6. Bywaters, E. G. L., and Beall, D.: Crush Injuries With Impairment of Renal Function, *Brit. M. J.* 1: 427-432, 1941.
7. Bywaters, E. G. L., and Delory, G. E.: Myohaemoglobinuria, *Lancet* 2: 649, 1941.
8. Colmers: Ueber die durch das Erdbeben in Messina am 28. Dec. 1908 verursachten Verletzungen, *Arch. f. klin. Chir.* 90: 701-727, 1909.
9. Doerr, R.: Die Anaphylaxieforschung im Zeitraum von 1914-1921. *Ergebnisse d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap.* 5: 72-274, 1922.
10. Duguid, J. B.: Primary Lesion in Phosphate Nephritis, *J. Path. & Bact.* 43: 321-326, 1936.
11. Dunn, J. S., and others: Renal Lesions in Two Cases of Crush Syndrome, *Lancet* 2: 549, 1941.
12. Dunn, J. S., Haworth, A., and Jones, N. A.: Urea Retention in Experimental Oxalate Nephritis, *J. Path. & Bact.* 27: 377-400, 1924.
13. Dunn, J. S., and Polson, C. J.: Experimental Uric Acid Nephritis, *J. Path. & Bact.* 29: 337-352, 1926.
14. Frankenthal, L.: Ueber Verschüttungen, *Virchow's Arch. f. path. Anat.* 222: 332-345, 1916.
15. Frankenthal, L.: Die Folgen der Verletzungen durch Verschüttung, *Beitr. z. klin. Chir.* 109: 572-587, 1918.
16. Froehner: Lehrbuch der Pathologie und Therapie der Haustiere, Stuttgart 1: 353, 1904.
17. Further Cases of Crush Injury Collected by Medical Research Council Subcommittee on Traumatic Oedema, *Brit. M. J.* 1: 449-451, 1941.
18. Giese, E.: Experimentelle Untersuchung über Erfrierung, *Vierteljahrsschrift. f. ger. Med., ser. 3*, 22: 235-263, 1901.
19. Groll: Direkte Kriegserkrankungen durch gröbers physikalische Einwirkungen, *Schjernings Handbuch d. Aerztl. Erfahrungen im Weltkrieg*, vol. 8, 1921.
20. Guenther, H.: Ueber den Muskelfarbstoff, *Virchow's Arch. f. path. Anat.* 230: 146-178, 1921.
21. Hackradt, Adolf: Ueber akute, todliche, vasomotorische Nephrosen nach Verschüttung. (München) 43 pp. 8°. Berlin, 1917, L. Schumacher.
22. Henderson, R. G.: Recovery From Uræmia Following Crush Injury, *Brit. M. J.* 2: 197, 1941.
23. Kitt: Lehrbuch der pathologischen Anatomie der Haustiere, Stuttgart, F. Enke 2: 423, 1911.
24. Krehl-Marchand: Handbuch der allgemeinen Pathologie, S. Hirzel, Leipzig, Bd. 1, 1908.

This list of authors, as well as many equally well known in other fields, gives assurance of the authoritative character of the reviews. Obviously, too, as the title implies, key indices to pertinent current literature are included. This monograph complements, in a useful manner, the year books published in the various specialties. This reviewer believes this effort of the authors, editor, and publisher to be a worthwhile endeavor which should be continued from year to year.

Psychosurgery. By Walter Freeman and James W. Watts. Pp. 337. Springfield, Ill., 1942, Charles C Thomas, Publisher.

This challenging monograph is devoted to the operative treatment of patients with intractable psychoses. Part I gives an interesting historical account of the early efforts of surgeons to deal with mental disorders, from the primitive trephining of the Incas down to the random cortical resections of Burekhardt in Switzerland, fifty years ago. It remained for Pusssepp in Estonia and Egas Moniz in Portugal to develop a more rational plan of interrupting the frontal association fibers. Part II takes up the anatomic-physiology of the frontal lobes and their connections, through the frontal association pathways, with the medial dorsal nucleus of the thalamus and other portions of the brain. The function of the frontal association areas has been arrived at from many angles and the authors' description of psychologic observations made after experiments on lower animals, frontal lobe softening, atrophy, wounds, and the effects of lobectomy in man is a particularly valuable review of this field.

In Part III Freeman and Watts describe the technical improvements they have made in the Moniz method of frontal lobotomy. With the original "leucotome," transection of the entire frontal radiations was uncertain and it soon became obvious that there are definite hazards in transecting the fiber tracts from above. The authors' present technique of making bilateral trephine openings (through the coronal suture and 6 cm. above the zygome) and cutting across a wide pie-shaped section of white matter with a straight, blunt instrument permits a surer and safer division of the association fibers. The operation is carried out under regional anesthesia, which permits continued observation of the psychologic reactions of the patient. These are described in interesting detail and special emphasis is laid on the fact that the surgical transections must be made to a sufficient extent to produce drowsiness on the operating table. Freeman and Watts' method, however, is not free from certain risks, as three patients have died as the result of postoperative clots and a similar number have developed epilepsy.

The authors begin their work with the obvious, although unfortunately not generally accepted, assumption that psychiatric disease is brain disease. To this is added a second assumption, namely, that brain surgery is therefore a reasonable therapeutic approach. The interesting points in the book from the psychologic point of view are: (1) the changes during operation, (2) changes of thinking and behavior caused by the operative lesion, (3) changes in the patient's illness following operation, that is, the therapeutic results.

It is striking that a change in the patient's state of awareness of his surroundings and ability to report on it takes place only after the operative lesion has been made in upper and lower quadrants bilaterally. The end point for the "complete" operation is a psychologic, not an anatomic one, that is, confusion or impaired ability to respond on the part of the patient.

As a result of operation there are certain noteworthy common changes in the patients: (1) loss of ambition and drive, (2) change in emotional attitude, and (3) deterioration in social habits. The authors describe "lack of initiative," "procrastination," "slowness, laziness, dullness, fatigability, euphoria, apathy, fecklessness, irritability," "thoughtlessness, poor judgment, sarcasm," and "impulsive acts,"

Book Reviews

A Manual of the Treatment of Fractures. By John A. Caldwell, M.D., Professor of Clinical Surgery, College of Medicine, University of Cincinnati; Director of the Fracture Service, Cincinnati General Hospital. Pp. 150, with 76 illustrations. Springfield, Ill., 1941, Charles C Thomas, Publisher. \$3.50.

This small concise manual of the treatment of fractures is probably the best of the several such books that have been published in the past few years. It fills adequately the need of medical students, house officers, and the general practitioner for a small but up-to-date authoritative textbook for rapid reference. It adheres to the recognized orthopedic principles and makes clear what leading contemporary authorities consider good practice in the treatment of fractures.

The illustrations are ample, to the point and diagrammatic. Unfortunately, there are no roentgenographic reproductions.

At the end of each chapter there is included a short list of references to the pertinent literature which should be of value to the student wishing to review the original sources. The book can be recommended as a welcome addition to our teaching armamentarium.

Synopsis of Genitourinary Diseases. By Dodson, Austin I., M.D., F.A.C.S. Ed. 3. Pp. 302. St. Louis, 1941, The C. V. Mosby Co. \$3.50.

This small, compact text is, as its name implies, a condensed handbook on urology. For lack of space, many theoretical considerations and alternatives of treatment are necessarily omitted, but it must be emphasized that nothing of any real practical value is left out. Also, surgical technique and postoperative care of surgical cases do not come within the scope of such work, and properly so, since it is designed purely as a handbook or guide in the management of office urologic practice.

The present edition is the third, and appeared last year, indicating the Dr. Dodson has revised and brought the book completely up to date, as regards recent advances in treatment.

All in all, this little text can unhesitatingly be recommended to all students and general practitioners of medicine as perhaps the finest work of its kind, in bringing to them in easily accessible manner, the innumerable bits of information necessary to the office practice of urology.

Medical Progress Annual 1940. A series of fifty-two reports published during 1940 in the *New England Journal of Medicine* under the managerial editorship of Robert N. Nye. Pp. 625, with 8 illustrations. Springfield, Ill., 1941, Charles C Thomas, Publisher.

Their monograph presents an excellent group of papers, requested from the *New England Journal of Medicine*, written by foremost men in their respective fields. The book embraces most of the specialties of medicine. A number of papers of great interest to the surgeon are included: A. W. Allen writes on "Progress in Abdominal Surgery"; W. E. Ladon on "Children's Surgery"; C. M. Jones on "Gastroenterology"; J. D. Stewart on "The Nutritional Requirements in Obstructive Jaundice"; R. H. Smithwick on "Surgery of the Sympathetic Nervous System"; and E. D. Churchill on "Progress in Thoracic Surgery."

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Original Communications

THE APPLICATION OF PHLEBOGRAPHY TO THE THERAPY OF THROMBOSIS AND EMBOLISM

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INCREASING clinical interest in the problems of thrombosis and embolism has led to the frequent use of phlebograms, not only for diagnosis, but, in many cases, to furnish necessary preoperative information. While a few sporadic radiographic studies of the venous system were made in the Massachusetts General Hospital in the past, our experience has been gained almost entirely within the last year. During this period phlebograms of slightly over 100 lower extremities have been made by various members of our peripheral vascular clinic. It has been possible to check anatomically the accuracy of the radiographic interpretations in many of these cases, since, to this date, seventy-three patients have had exploration and ligation of the femoral vein performed (nine of this latter group had bilateral ligations).

Great credit must be given to dos Santos¹ and to Bauer² for their introduction and elaboration of the phlebographic technique, with its application to the disease of thrombo-embolism. After studying their monographs, it is easy to become extremely enthusiastic about the method. Critical evaluation has substantiated many features, but has also discovered certain limitations that must be recognized. Some of the problems that have developed have been noted by Dougherty and Homans,³ but are important enough to merit further discussion.

METHODS

The first problem involves the production of an accurate phlebogram. This should demonstrate, so far as possible, the patency or block of all

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as examples of change or loss. In other words, new symptoms are produced and presumably mark an improvement over the symptoms of the patient's illness. Neurologic sequelae have included: inertia, masked facies, convulsions, hemiparesis, aphasia, and ataxia. Permanent change with respect to the above symptoms is less common than temporary change.

Most of the cases subjected to this operation were diagnosed affective reaction types (38 cases) or tension states (19 cases). High degree of persistent relief is reported for the symptoms: nervous tension, worry, anxiety, insomnia, suspiciousness, apprehension, agitation; for crying spells, suicidal ideas, depersonalization, frigidity, irritability; for introversion, indecisiveness, negativism, delusions, ideas of influence or reference. Therapeutic results reported of the affective reaction type group (38 cases): 26 patients, good; 6, fair; 4, poor; 1, dead; and 1, unevaluated. Of the 19 tension state cases: 14, good results; 1, fair; 2, poor; 2, dead. Of the 12 patients with schizophrenia there were: 5, good; 4, fair; 2, poor results, and 1, unevaluated. A few cases of psychoneuroses (anxiety state or hysteria), alcoholism, and of unclassified psychoses were operated upon with good results reported for the psychoneuroses.

The book makes interesting reading and the theories and speculations it presents are highly stimulating. Most plausible is the general concept that the thalamus represents the emotions and the cortex the ideas and plans. Cutting the connections of the cortex and thalamus thus separates worry from thinking, but unfortunately also separates drive from planning, concern with good manners from social behavior.

Two important questions are left unanswered. First, just what anatomic structures are destroyed in the operation? The fact that the part of the brain cut is not seen by the operator and the fortunately small number of deaths account for this. Serial sections of the brain at a later date will clarify this point. Second, is the operation of benefit to patients? The evaluation of therapeutic results in psychiatric disease is a difficult one. A systematic presentation of protocols of *all* cases operated would have been valuable in assisting the reader in evaluating the therapeutic possibilities of the operation. Space for this presentation might have been obtained by judicious omission of some of the theorizing about the causes of the illnesses, since the illnesses described are all diseases of unknown etiology. Whether or not the disability occasioned by the operation will in time outweigh the loss of symptomatology, the future will decide. Whether the operation or the passage of time occasioned improvement is also a major problem to be answered. Even without any treatment, the prognosis in patients with involutional melancholia featured by much anxiety and tension is good, according to some observers. If this be true, the problem of therapeutic evaluation here is exceedingly difficult.

On the whole the book is well worth reading by those interested in psychiatry, cerebral function, and experimental surgery on the human brain.

femoral vein had been obliterated by the phlebitic process. However, clinical tests have made us certain, in nearly all cases we have observed, that the femoral vein is patent. Absolute permanent obliteration of the femoral vein must be extremely rare.

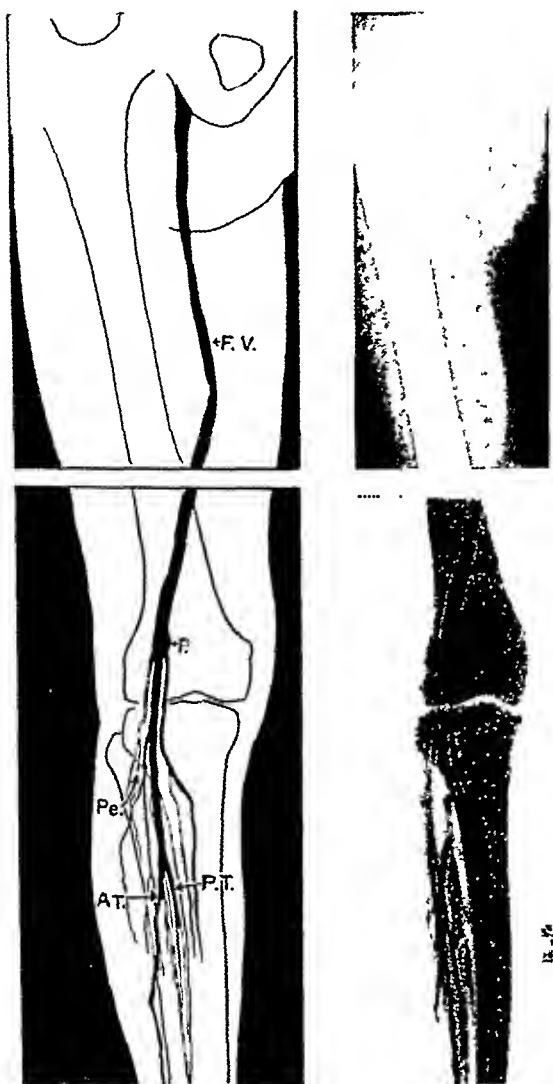


Fig. 1.—P. W., normal phlebogram. Note the femoral vein (F.V.) in which valves can frequently be seen, the popliteal vein (P.), and numerous branches in the lower leg, of which the most important are the anterior tibial (A.T.), posterior tibial (P.T.), and peroneal (Pe.).

It appears, therefore, that preferential return of the diodrast by way of the long saphenous vein, if the patient has had previous deep phlebitis, may lead to an erroneous impression concerning the patency of the femoral vein. To obviate that objection, the next method was employed.

parts of the venous system of the extremity. We have used several different methods, varying in so far as the site and method of injection are concerned. The details of the radiograph and of the medium employed have been the same in all instances. The methods are as follows:

1. In the early cases Bauer's technique was used as a routine method. After novocain infiltration, a 2 cm. incision at right angles to the Achilles tendon, just behind the external malleolus, is made. The terminal branch of the short saphenous vein is isolated in the subcutaneous tissue. A No. 18 ball-pointed needle, inserted proximally, is tied into the vein. The patient is then placed flat on his back with the heel elevated on a four-inch block. The leg is internally rotated ten to fifteen degrees to secure the widest gap between the tibia and fibula when the picture is taken. Two large x-ray cassettes are placed in tandem beneath the leg. The lower should extend a short distance above the knee, since a short blank space will appear between the two cassettes, and should not include this important area. The focal length of the tube must be about six feet, since the entire leg must be included in the field. Twenty-five cubic centimeters of diodrast are then injected at a steady rate, so that exactly sixty seconds are consumed. At this time, just at the conclusion of the injection, using soft-tissue technique, the x-ray exposure is taken. A normal phlebogram obtained in this manner is shown in Fig. 1.

The advantages of Bauer's technique are that the same vein is used in all instances so that all phlebograms are comparable in that respect. Occasionally it is difficult to isolate the terminal branch of the short saphenous vein and requires a minor operative procedure. A more important criticism is that the deep venous system may not be delineated accurately. An interesting case brought this to our attention.

E. W. (M. G. H. No. 208227), a 62-year-old female, entered the hospital because of varicose veins. She gave a history of phlebitis on the right (twenty-five years previously), followed by mild chronic swelling, but no ulceration. In order to determine the status of her deep venous system, a phlebogram (Fig. 2A) was done by the method of Bauer. Apparently there was complete block of the deep veins, the diodrast returning entirely by the long saphenous vein. Clinical tests, however, indicated that the femoral vein was not occluded and the long saphenous vein was incompetent. Accordingly, the saphenous vein was ligated at the sapheno-femoral junction. A day thereafter, a repeat phlebogram (Fig. 2B) showed that the deep venous system was patent. Irregular filling of the femoral vein indicated that the vein had been recanalized after the previous attack of phlebitis.

Thus, absence of filling of a deep vein may be due to the preferential return of dye by another route. The patients who have a long history of deep phlebitis and have developed long saphenous varicosities often present a confusing picture. Phlebograms will usually show no filling of the femoral vein with the long saphenous or other collateral veins clearly outlined. Bauer believed that this meant the

phlebogram. This can, however, be almost surely detected clinically because of the superficial location of the vein. It is important also to note that a pressure of as much as 40 mm. of mercury may be necessary to occlude some sclerosed, varicose saphenous veins completely, but that too great a tension in the cuff may compress the deep as well as the superficial system.

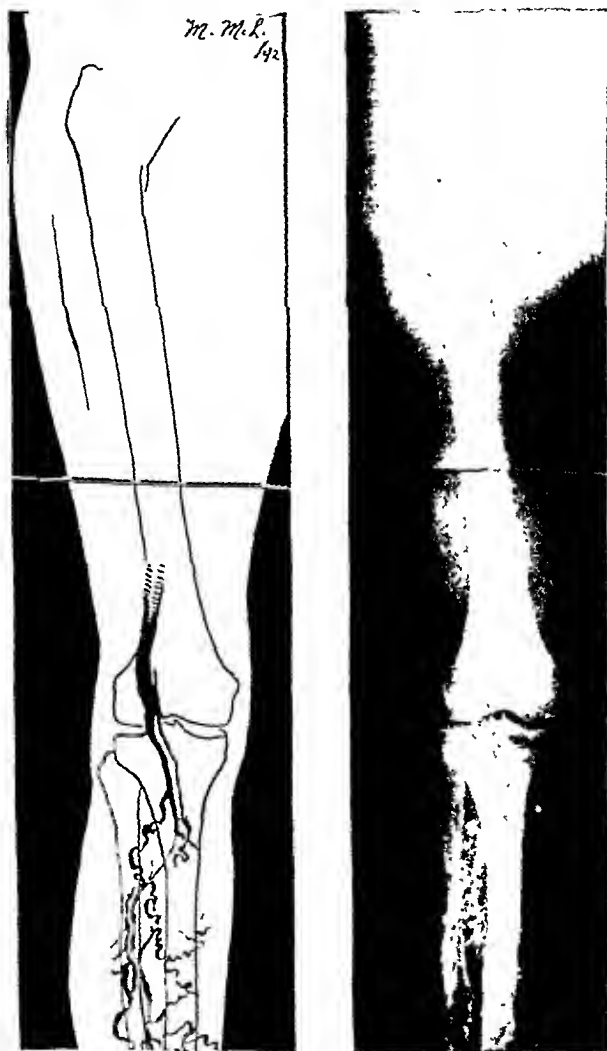


Fig. 2B.—E. W. (M. G. H. No. 208227), postoperative phlebogram. After high saphenous ligation, the phlebogram demonstrates a patent popliteal and lower femoral vein.

3. The injection is made into one of the dorsal veins of the foot, or the distal end of the long saphenous vein. Return of blood through the

2. The technique is the same as that of Bauer, except that a blood pressure cuff with a pressure of 20 mm. of mercury is applied to the lower leg, the upper level being at the mid-calf. Accordingly, the long saphenous vein is occluded by the tourniquet so that all of the injected diodrast must flow through the deep femoral system.

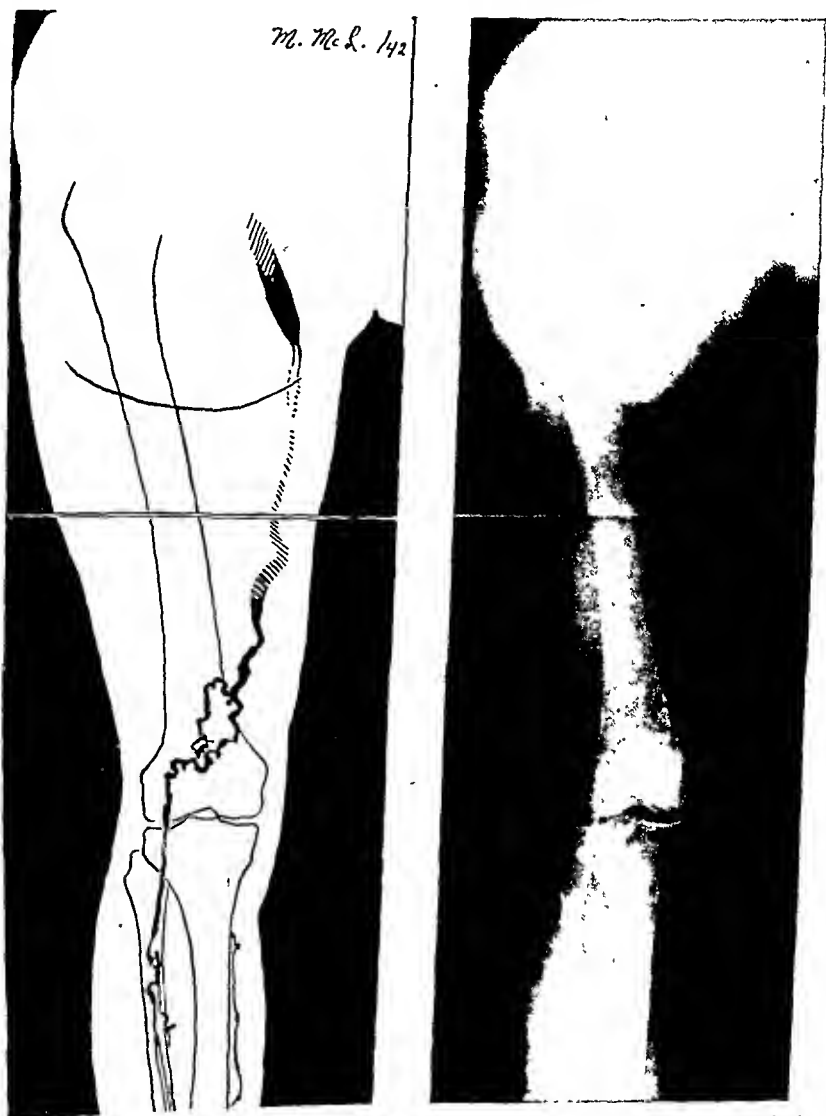


Fig. 2A.—E. W. (M. G. H. No. 208227), preoperative phlebogram. Deep phlebitis twenty-five years previously, incompetent long saphenous vein. Note the absence of filling of the deep venous system. Diodrast outlines only superficial veins and the long saphenous vein in the thigh.

Use of this method means that the presence or absence of thrombosis in the long saphenous vein cannot be determined accurately from the

INDICATIONS

In general phlebograms are valuable (1) in any case of known or suspected thrombosis of the veins of the lower leg, or (2) after a pulmonary infarct has occurred, unless it unquestionably has arisen from



Fig. 3A.—J. B. (M. G. H. No. 276333). Phlebogram taken two hours after onset of deep phlebitis revealed no definite evidence of thrombosis.

long saphenous vein is prevented by the use of a tourniquet as described above. Prompt filling, primarily of the posterior tibial vein by means of numerous perforating vessels in the lower leg, is obtained.

This method, suggested by Linton,⁴ is the simplest to employ, and has produced radiographs that are as accurate as those produced by the more cumbersome procedure.

All of these methods are subject to certain theoretical objections. In the first place, it seems improbable that all the main venous channels could be filled by injection of the terminal end of either the long or short saphenous vein, despite the presence of numerous communicating veins. Also, the venous pattern in the lower leg is not constant enough to make it possible to be certain that thrombosis is present when only a portion of one of the main veins has been thrombosed. Further, if the thrombosis has originated in one of the muscular veins of the calf, as the studies of Hunter, Sneed, Robertson, and Snyder⁵ have shown is the most common source, or in the plantar veins, the phlebogram will not become positive until the major venous channels are involved.

It follows that in certain instances thrombosis of certain veins of the lower leg may exist despite an apparently normal phlebogram. The clinical diagnosis of thrombosis was made in three of our patients at a time when the phlebogram showed normal filling of the main veins. At a later date, the occurrence of emboli led to a repetition of the phlebogram, which was positive in the three cases.

J. B. (M. G. H. No. 276939) was a 45-year-old man who had a laminectomy for the removal of a ruptured intervertebral disc on April 16, 1941. Ten days after operation he had the sudden onset of tenderness in the left calf and over the course of his femoral vein to the groin, and a positive Homans' sign. No edema was present. A phlebogram done two hours after onset (Fig. 3A) showed no definite abnormality. In view of this finding the patient was heparinized and within twenty-four hours his leg symptoms had entirely disappeared. Seven days later, after a continued irregular temperature record, he had signs of pulmonary infarcts, later confirmed by x-ray. Re-evaluation of the legs proved them to be again entirely negative clinically. However, bilateral phlebograms were done which proved the right to be normal, but the left leg now showed the femoral system to be occluded (Fig. 3B). Femoral exploration confirmed the femoral thrombosis. Some free thrombus was removed and the vein ligated. The patient recovered with no further difficulty.

It seems, therefore, that the phlebogram cannot be considered absolutely reliable in so far as the diagnosis of thrombosis is concerned. Certainly there are many cases in which a leg appears clinically normal, while the phlebogram will show the presence of a deep thrombosis. On the other hand, if clinical signs indicate that thrombosis is present, and if the phlebogram is indeterminate or negative, the patient should be considered to have thrombosis, and therapy should be determined on that basis.

We have expected that certain systemic manifestations might occur after the injection of the 50 c.c. of diodrast that are required for the production of bilateral phlebograms. Up to the present time, none has occurred. It has been suggested that the chemical irritation of a vein by the diodrast may be sufficient to initiate venous thrombosis. Another objection raised is that thrombi might be mechanically dislodged by the introduction of the diodrast. It is possible that both of these objections are valid in rare instances; we have not, however, seen any evidence to support them, and are convinced that the practical results completely outweigh these theoretical considerations.

One contraindication to a phlebogram is the presence of sepsis about the ankle. Usually some vein in normal tissue can be utilized, but occasionally none is available.

APPLICATION

The phlebogram, to be considered of any important value, must furnish information that is not demonstrable by astute clinical examination. Of course it does provide, in addition, a permanent record of the extent of the thrombosis that is of importance in the study of any series of cases.

The inaccuracy of clinical examination in any case of thrombosis is notorious, and has been discussed so frequently that it is unnecessary to do so again. It has already been pointed out by Fine and Sears⁶ that many previous studies of thrombo-embolic problems have been entirely misleading since the venous systems involved have not been noted accurately.

Certain groups of cases demonstrate the value of the phlebogram most clearly. They will be illustrated by case reports:

1. The diagnosis of thrombosis is important, even though no specific therapy is contemplated. Occasionally a patient in his postoperative course will develop fever and elevated pulse. Other possible complications may be ruled out, and the diagnosis of thrombophlebitis made by a phlebogram.

F. G. (M. G. H. No. 305431) was a 22-year-old female who was admitted to the hospital for an elective cholecystectomy. Two weeks after operation, just after the common duct tube was removed, she began to run a temperature of 102° F. It was believed that she was developing a subdiaphragmatic abscess. Two days later slight tenderness in the left groin, and a one-inch increase in circumference of the thigh suggested the possibility of deep phlebitis. The diagnosis was established by means of a phlebogram (Fig. 4) which showed a block of the femoral vein. No further investigations of the subdiaphragmatic area were made and the patient was treated conservatively for the phlebitis, because of her youth. She recovered without incident and left the hospital two weeks later.

2. Pulmonary infarcts have occurred, with no evidence of the source. Phlebograms of the legs may show the source of the emboli, and ligation of the femoral vein will result in cure.

elsewhere than the leg. Because thrombosis is so frequently bilateral, many patients will require bilateral procedures. The two phlebograms

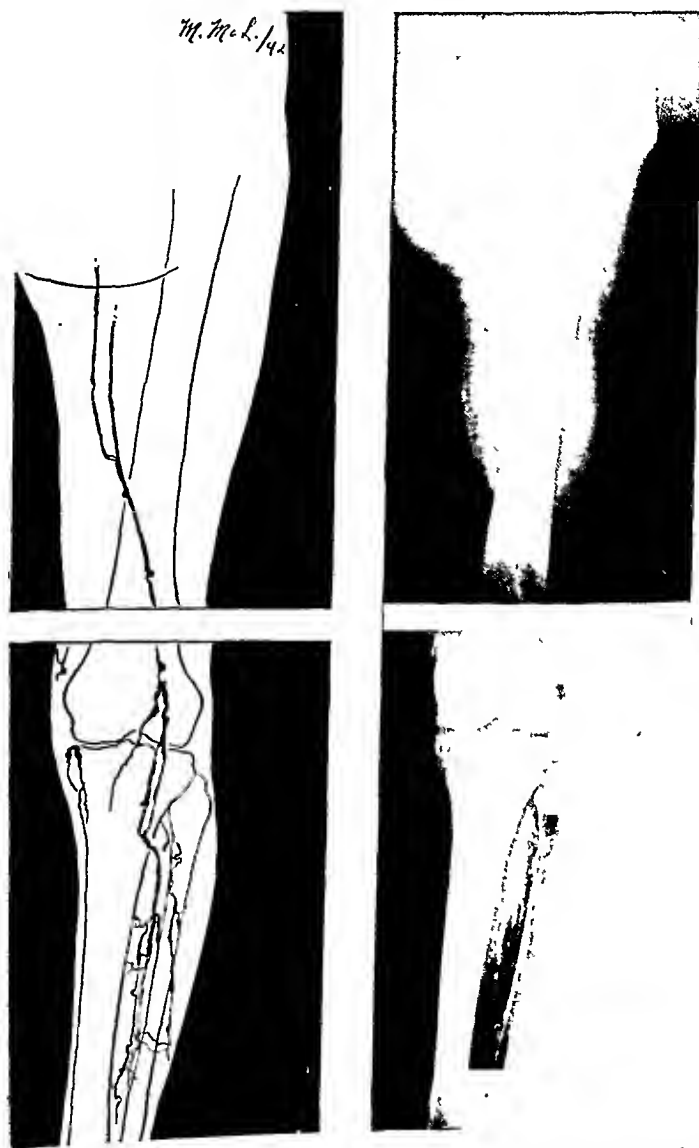


Fig. 3B.—J. B. (M. G. H. No. 276939). Phlebogram done two weeks after that shown in Fig. 3A. Observe obliteration of the femoral vein with return of diiodrast by collateral vessels.

may be taken one after the other without risk. The existence of a superficial thrombophlebitis constitutes a special indication for a phlebogram, since involvement of the deep system will be found to occur quite commonly in conjunction with thrombosis of the saphenous vein.

culture for pneumococcus obtained. Two weeks after admission an x-ray showed an area of consolidation in the right lower lobe, and five days later, a process lateral to the hilum on the left, which was interpreted as a pulmonary infarct. Shortly thereafter, his status improved and he was allowed out of bed. He then, for the first time, complained of a little pain over the left calf and measurements showed three-fourths of an inch swelling on the left, with negative Homans' sign. Since no previous observations had been made of the circumference of his legs, it was uncertain whether or not this finding was of consequence. On the other hand, his phlebograms were striking for they showed filling along the course of a clot in the femoral vein, the head of which was just above the mid-thigh (Fig. 5). Exploration of the femoral vein was carried out at this level and a clot was found incompletely fixed to the vein wall. Following this he recovered rapidly and was discharged.

3. An acute superficial thrombophlebitis is present. A phlebogram of the involved extremity is indicated. Frequently an associated, widespread thrombosis of the deep venous system will be found.

J. L. (M. G. H. No. 299805), a 63-year-old man, had a two-stage resection of the rectum for carcinoma. Nine days following the second stage, he developed an area of swelling and redness over the course of the left long saphenous vein in the region of the knee. Homans' sign was negative and measurements of the legs were equal except below the knee at the level of the localized obvious swelling. Here the leg was one inch larger. During the next twenty-four hours the superficial phlebitis progressed to above the knee, though the swelling remained localized. We had discussed the use of phlebography prior to this case and although all the evidence pointed to a superficial process, we made our first phlebogram on this man (Fig. 6). Much to our surprise, there was occlusion of the entire deep venous system. Femoral exploration proved the presence of a large, soft thrombus which extended above the sapheno-femoral junction. This was removed and the vein ligated. Recovery was uneventful.

4. The presence of a deep thrombosis is suspected and immediate therapy is contemplated. The early detection of thrombosis is essential if treatment is to be instituted before emboli have occurred. Hence, phlebograms are performed as emergency procedures day or night on the slightest indication. Many different types of pictures are obtained. The most common are as follows:

(a) Massive thrombosis of all main deep venous channels. In the usual case, practically no veins are visible on the x-ray plate. All the diodrast that is injected fills a constricted saphenous vein, and the deep veins are not visible at all. This was the most common picture obtained early in the study when phlebograms were often delayed many hours for various considerations; it is a later stage of thrombosis. Exploration of the femoral vein will usually reveal recently formed thrombus in the common femoral and external iliac veins. The thrombus must be removed by the Trendelenburg suction device before ligation of the vein.

J. O. (M. G. H. No. 336852) was a 66-year-old man who had a spontaneous onset of throbbing pain in his right instep and sole of his foot eight days before entry.

T. K. (M. G. H. No. 235921) was a 55-year-old man with long-standing rheumatic heart disease and fibrillation, who was admitted to the medical service with a diagnosis of bronchopneumonia. He had had "grippe" one week previously and had

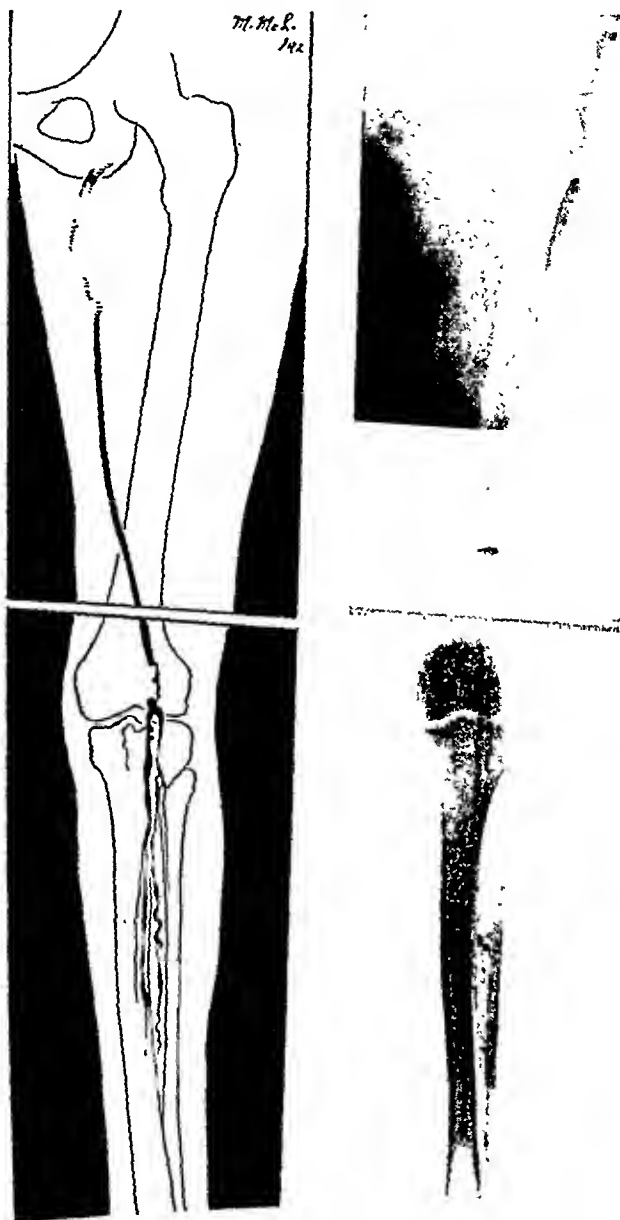


Fig. 4.—F. G. (M. G. H. No. 305431). Note the obliteration of the femoral system.

raised blood-streaked sputum for three days prior to admission. The x-ray showed a poorly defined area of density thought to be consistent with lobar pneumonia. During the next four weeks his course was irregular but at no time was a positive

large clot with a free-lying tip was extracted from the proximal end of the vein. The common femoral vein was divided and ligated. The patient recovered without complication and left the hospital ten days later.

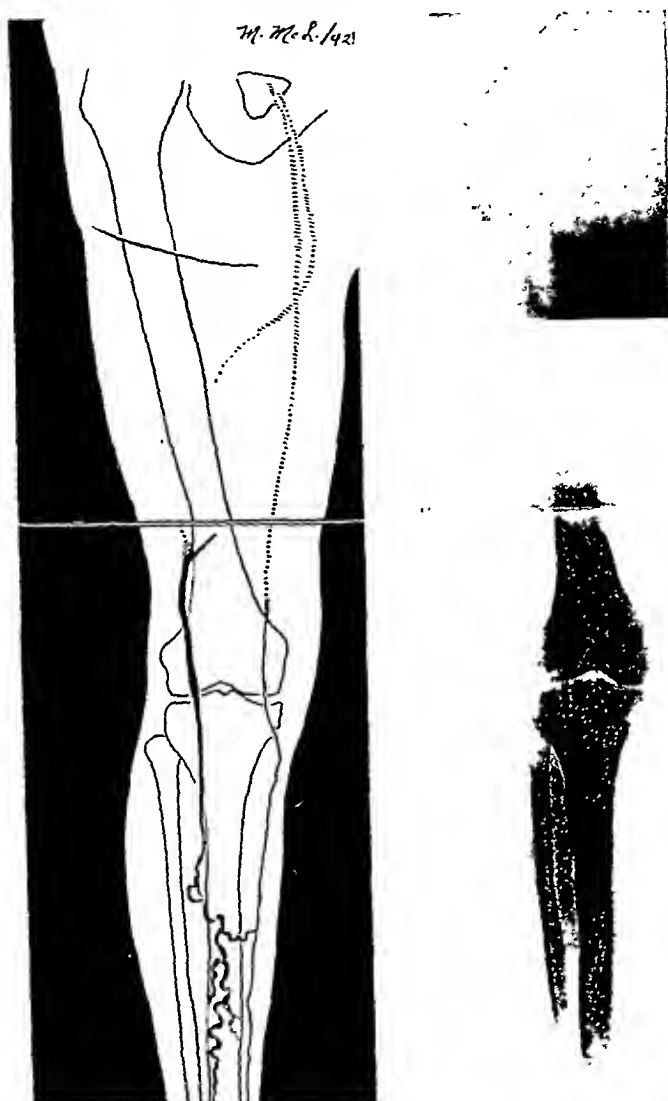


Fig. 6.—J. L. (M. G. H. No. 28965). Acute superficial and deep thrombophlebitis. Note the almost complete lack of filling of veins and the total absence of the normal pattern.

(b) Thrombosis of the veins of the calf. One or all of these vessels may be thrombosed. If all are thrombosed, interpretation is easy, but if only one vein is not filled, the radiographic interpretation is likely to vary with different observers. A phlebogram of the opposite leg is especially valuable as a control in this group of cases.

Shortly thereafter, slight swelling developed in his foot and his podiatrist recommended new shoes. In spite of this, pain and swelling persisted, and he then consulted his physician, who ordered rest and hot water bottles to the leg. Since



Fig. 5.—T. K. (M. G. H. No. 235021). There is complete thrombosis of the lower two-thirds of the femoral vein and partial filling in the lower leg.

there was no improvement, he was admitted to the hospital. No tenderness was elicited along the superficial or deep venous trunks. A phlebogram (Fig. 7) revealed typical deep venous occlusion which was confirmed by femoral exploration. A

ligated and found to be patent. The patient later survived resection of the colon and duodenum, leaving the hospital eight weeks after his vein ligation, with no other thrombo-embolic complication.

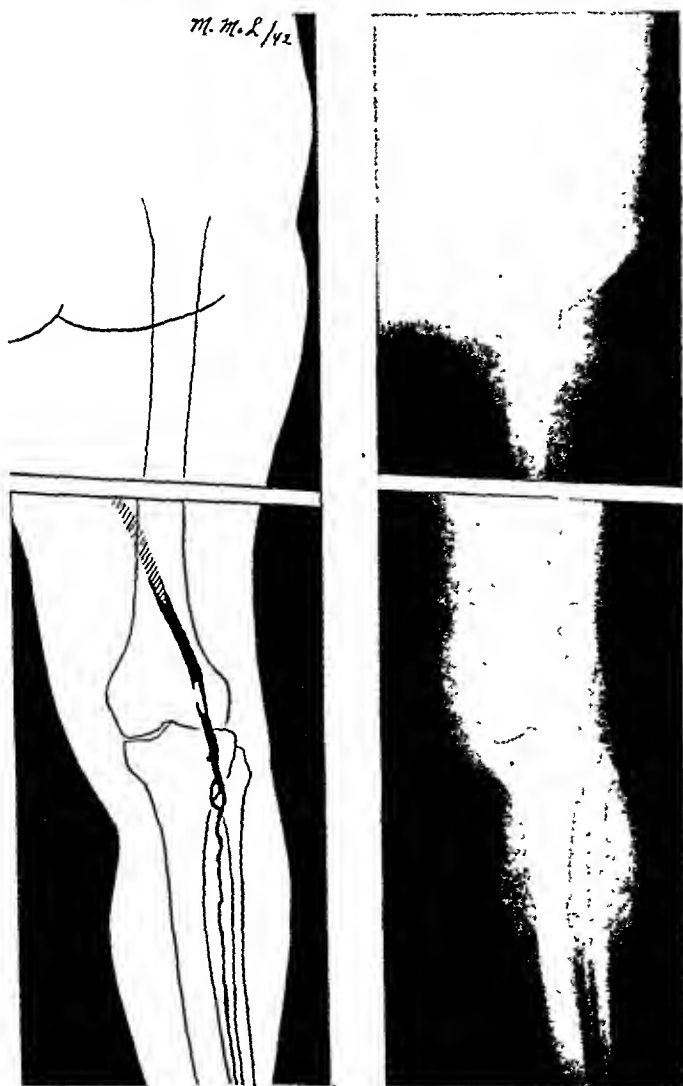


Fig. 5-T 1 (M. G. H. No. 319658) Early deep phlebitis of the lower leg. No filling of the posterior tibial vein. The upper femoral vein was not visualized because of an insufficient amount of diodrast.

In this group, the thrombosis has been recognized at an early stage. The superficial femoral vein may be ligated and the patient may be allowed out of bed at once with no fear of embolism.

(c) The popliteal and lower femoral veins are partially thrombosed. This is a stage intermediate between (b) and (a). Occasionally a loose

T. I. (M. G. H. No. 319658), a 47-year-old Polish woman, entered the hospital on Sept. 9, 1941 with an appendiceal abscess. On conservative management she improved steadily and became essentially afebrile by her fifteenth hospital day. She was then allowed out of bed for the next three days, but her temperature gradually rose to 100° F. During the afternoon of the third day, she complained of

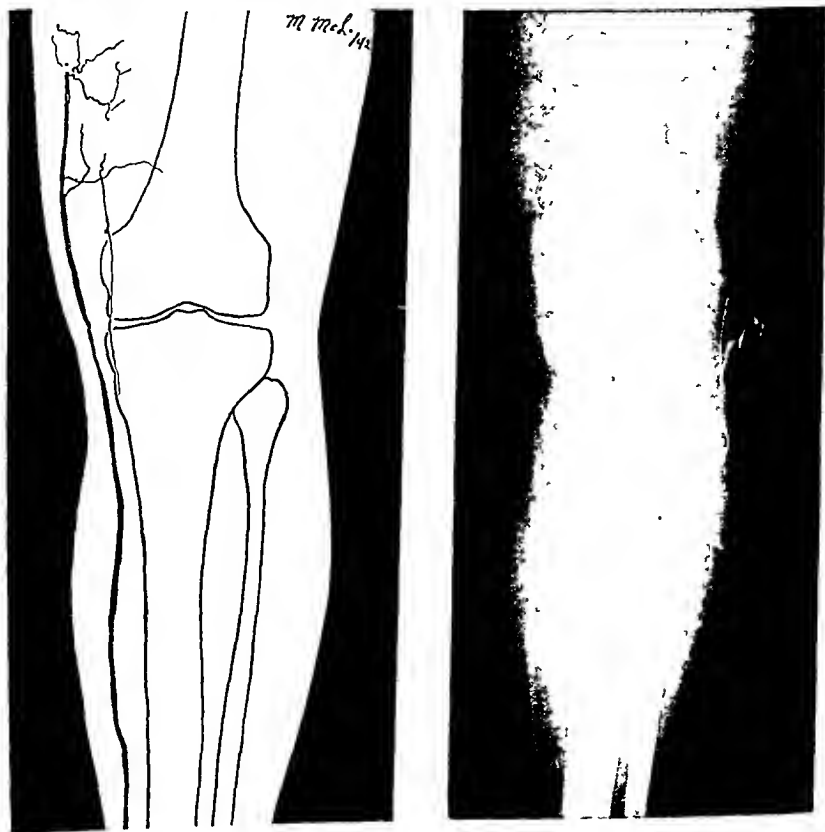


FIG. 7.—J. O (M. G. H. No. 336852). Acute deep thrombophlebitis. The long saphenous vein fills normally, but the deep system is not visualized

sharp, transitory pain in her left chest. The chest x ray was negative for infarct. The following morning the patient complained of pain low in the left calf. Examination revealed a well-localized area of tenderness over the Achilles tendon, but no measurable swelling. The tissues over this level felt thickened. A phlebogram (Fig. 8) showed obstruction of the posterior tibial vein. This patient refused any operative procedure and was discharged shortly.

P. B. (M. G. H. No. 329354), a 59 year-old male, had a two-stage resection of carcinoma of the hepatic flexure, complicated by a duodeno colic fistula. Ten days after his first stage, he developed fever, slight right calf tenderness, and two-inch swelling of the right calf. The right femoral vein was explored after the phlebogram demonstrated complete deep venous occlusion and a large, soft thrombus was removed. The following day he had moderate swelling on the left side. Here the phlebogram demonstrated femoral patency, but block of the deep channels below the mid-popliteal level (Fig. 9). The left superficial femoral vein was immediately

oral vein will be observed. If a long saphenous phlebitis is present, this indicates that the thrombosis has extended by way of the communicating veins from the saphenous to the femoral vein. Such patients are especially prone to repeated attacks of small pulmonary emboli.

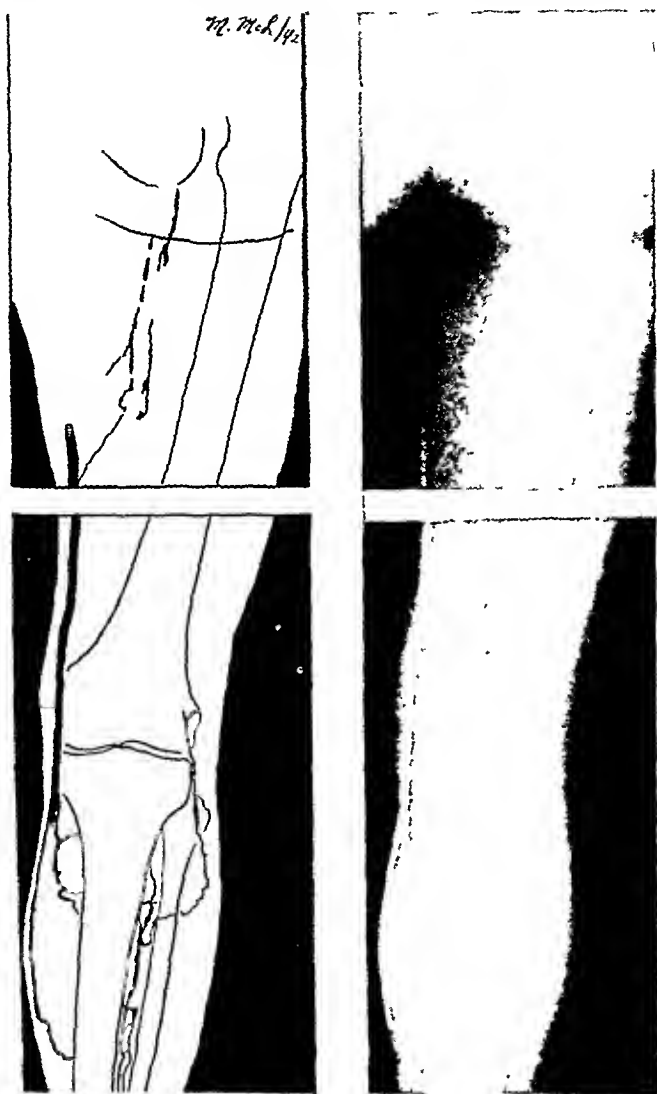


Fig. 10.—L. H. (M. G. H. No. 24371) Mantle filling showing the diiodrast escaping along an incompletely fixed thrombus in the upper femoral vein

Very rarely the phlebogram of the lower leg and popliteal veins may appear normal, with a large, loosely-attached thrombus in the femoral vein. This is an important type, from a theoretical point of view, since it proves that massive thrombosis of the crural veins does not always precede thrombosis of the femoral vein. These thrombi are floating in a

thrombus in the femoral vein is actually demonstrated by the diodrast passing around the thrombus. This has aptly been termed by Bauer "mantle filling." In this group of cases a loose clot can usually be withdrawn from the femoral vein. Embolic phenomena are especially common, are apt to be fatal, and can be prevented only by ligation of the vein.

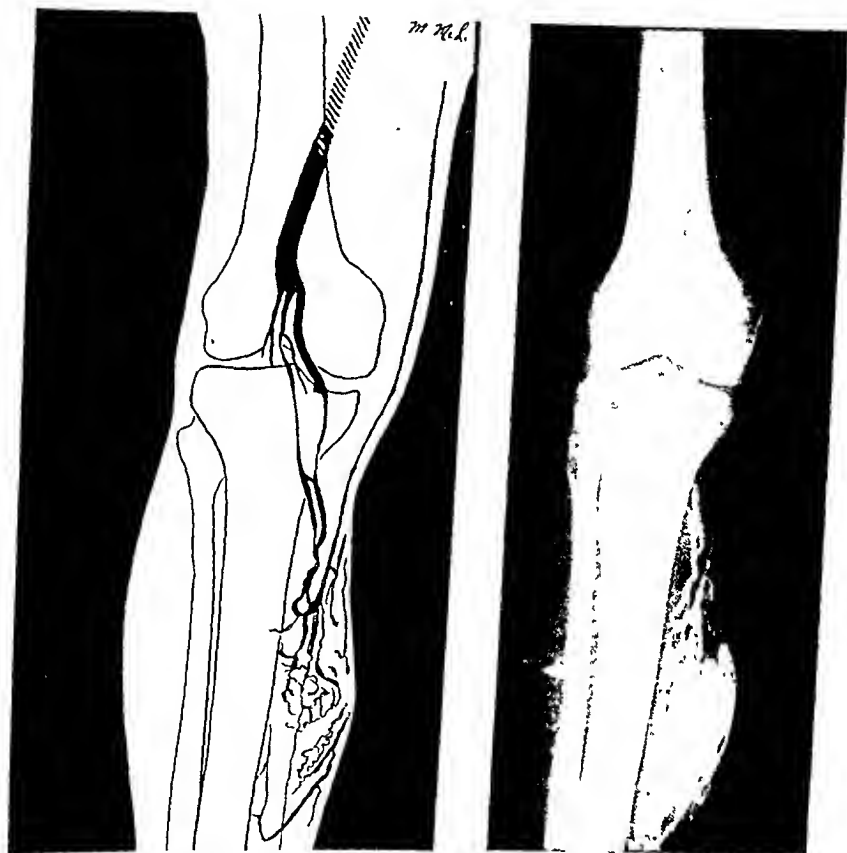


Fig. 9.—P. B. (M. G. H. No. 329351). Acute deep thrombophlebitis confined to the veins of the lower leg. Diodrast is seen in only the superficial veins and uppermost portion of the crural veins.

L. H. (M. G. H. No. 243171), a 39-year-old male, developed tenderness and pain in his left calf three days after drainage of a lung abscess. The calf was moderately swollen. His phlebogram (Fig. 10) showed incomplete block of the popliteal and femoral veins and demonstrated the escape of the diodrast along the periphery of an eel-like thrombus. Immediate exploration yielded a large, soft clot lying free in the common femoral, the head of which was recovered from the external iliac by introducing the Trendelenberg suction tip. The common femoral and saphenous veins were ligated and divided. Recovery was uneventful. Four months later, in the outpatient department, no swelling of the leg was demonstrated.

(d) Occasionally, the entire femorocrural system will not be found to be thrombosed, but mural thrombi involving only a portion of the fem-

and her fever lessened. After being up again for two days she had a return of the chest pain with fever to 100.6° F. Chest x-ray showed multiple small areas of pulmonary infarction over both lower lung fields. For the first time her left calf and ankle measurements were one-half to three-fourths of an inch greater than the right. No areas of tenderness were elicited, but the patient complained of a mild ache in the calf. Bilateral phlebograms were made showing normal filling on the right. In the upper femoral region on the left was a large mural thrombus (Fig. 11). Immediate femoral exploration confirmed this finding and a large, soft clot was aspirated from the distal segment of the femoral vein. The patient's course was subsequently uneventful.

THERAPY

The therapy of venous thrombosis will be considered only briefly. In our clinic we have attempted to evaluate venous ligations, chiefly because our incidence of emboli has been high. Thus, our control group showed one infarct out of every three cases of deep phlebitis, while the death rate of thrombo-phlebitis in patients over the age of 50 was nearly 8 per cent because of massive infarcts alone.⁷ The mechanical prevention of emboli by actual ligation was, therefore, especially appealing.

We have now ligated eighty-two femoral veins for deep venous thrombosis. Ligation is done in any case if the patient is 40 years of age or over, or if he is under 40 and has a bland thrombosis or has had a pulmonary infarct. Of the patients in the ligated group, the average age was 56. According to our control figures we should have expected that about twenty-five patients would have had further pulmonary infarcts, while six would have been fatal in this group if conservative therapy had been employed. However, after ligation we observed only two infarcts, one of which could not be confirmed by x-ray, and neither one of which was fatal. Bilateral ligations have been done nine times.

The site of ligation is very important and may be determined by the phlebogram. The vein should be ligated below a large branch in order to avoid a long static column of blood with potential thrombosis and fatal embolism. This means that ligation of the popliteal vein should not be done. Ligatures may be placed on the superficial femoral, common femoral, or iliac vessels. Since most of these operations are done in very ill patients, we have tended to make the procedure as simple as possible and have avoided the extra dissection required for iliac ligation, preferring to use suction to withdraw thrombi from higher levels. Practically, then, the decision must be made as to whether to ligate the femoral vein below the profunda branch, above the saphenous junction, or at some point between. It is advisable to ligate above the thrombosis if possible. If not, the vein must be opened over the thrombus and the clot extracted with a suction apparatus.

In certain cases the venous anastomosis above and below the site of ligation is poor. This had led in two cases to marked distention of the entire venous system of the extremity and to extravasation of blood into

rapidly moving column of blood, and are the most dangerous type of all. Immediate ligation is essential to prevent death from a massive embolus.

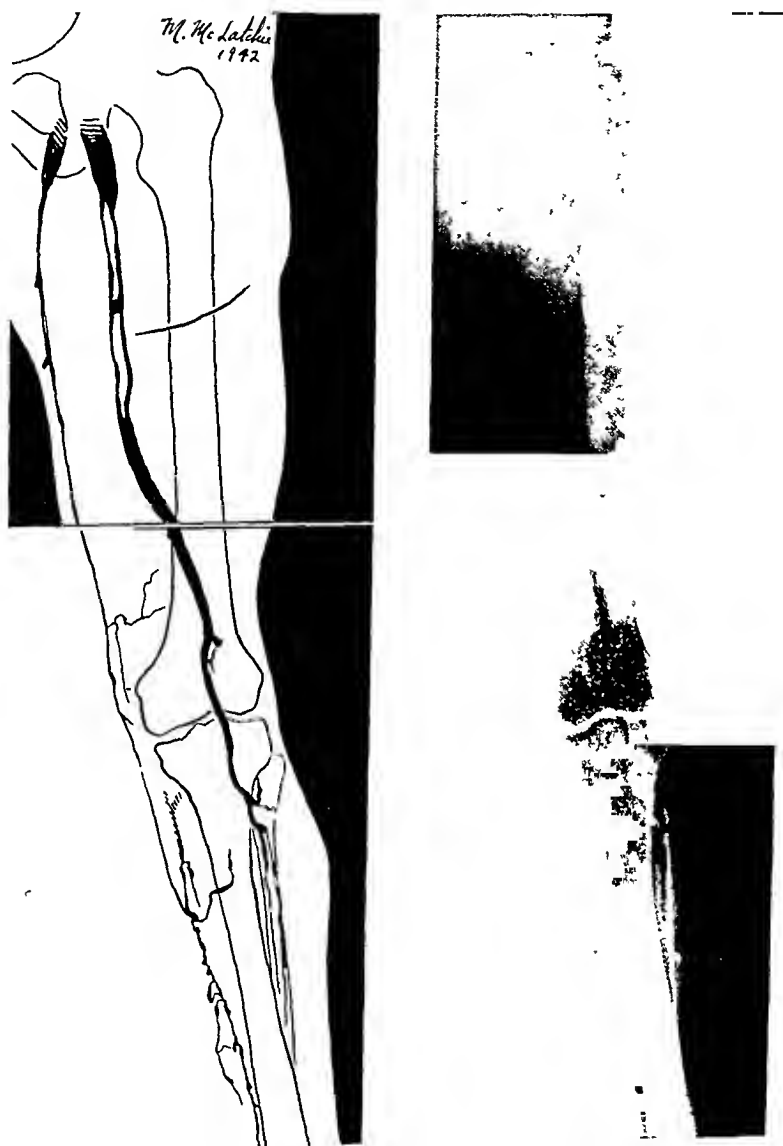


Fig. 11.—A. C. (M. G. H. No. 304502). Mural thrombus seen in the middle and upper portions of the femoral vein. Note deep system filling below.

A. C. (M. G. H. No. 304502), a 56-year old female, was operated upon Jan. 27, 1942, for a Dupuytren's contracture of the left hand. She was allowed to be out of bed for the first three postoperative days. The following day her temperature rose to 100° F. and twenty-four hours later she developed pleuritic pain over the right chest and a nonproductive cough. Chest x ray showed a high right diaphragm with linear atelectasis. During the next five days in bed the chest pain disappeared

and her fever lessened. After being up again for two days she had a return of the chest pain with fever to 100.6° F. Chest x-ray showed multiple small areas of pulmonary infarction over both lower lung fields. For the first time her left calf and ankle measurements were one-half to three-fourths of an inch greater than the right. No areas of tenderness were elicited, but the patient complained of a mild ache in the calf. Bilateral phlebograms were made showing normal filling on the right. In the upper femoral region on the left was a large mural thrombus (Fig. 11). Immediate femoral exploration confirmed this finding and a large, soft clot was aspirated from the distal segment of the femoral vein. The patient's course was subsequently uneventful.

THErapy

The therapy of venous thrombosis will be considered only briefly. In our clinic we have attempted to evaluate venous ligations, chiefly because our incidence of emboli has been high. Thus, our control group showed one infarct out of every three cases of deep phlebitis, while the death rate of thrombo-phlebitis in patients over the age of 50 was nearly 8 per cent because of massive infarcts alone.⁷ The mechanical prevention of emboli by actual ligation was, therefore, especially appealing.

We have now ligated eighty-two femoral veins for deep venous thrombosis. Ligation is done in any case if the patient is 40 years of age or over, or if he is under 40 and has a bland thrombosis or has had a pulmonary infarct. Of the patients in the ligated group, the average age was 56. According to our control figures we should have expected that about twenty-five patients would have had further pulmonary infarcts, while six would have been fatal in this group if conservative therapy had been employed. However, after ligation we observed only two infarcts, one of which could not be confirmed by x-ray, and neither one of which was fatal. Bilateral ligations have been done nine times.

The site of ligation is very important and may be determined by the phlebogram. The vein should be ligated below a large branch in order to avoid a long static column of blood with potential thrombosis and fatal embolism. This means that ligation of the popliteal vein should not be done. Ligatures may be placed on the superficial femoral, common femoral, or iliac vessels. Since most of these operations are done in very ill patients, we have tended to make the procedure as simple as possible and have avoided the extra dissection required for iliac ligation, preferring to use suction to withdraw thrombi from higher levels. Practically, then, the decision must be made as to whether to ligate the femoral vein below the profunda branch, above the saphenous junction, or at some point between. It is advisable to ligate above the thrombosis if possible. If not, the vein must be opened over the thrombus and the clot extracted with a suction apparatus.

In certain cases the venous anastomosis above and below the site of ligation is poor. This had led in two cases to marked distention of the entire venous system of the extremity and to extravasation of blood into

rapidly moving column of blood, and are the most dangerous type of all. Immediate ligation is essential to prevent death from a massive embolus.

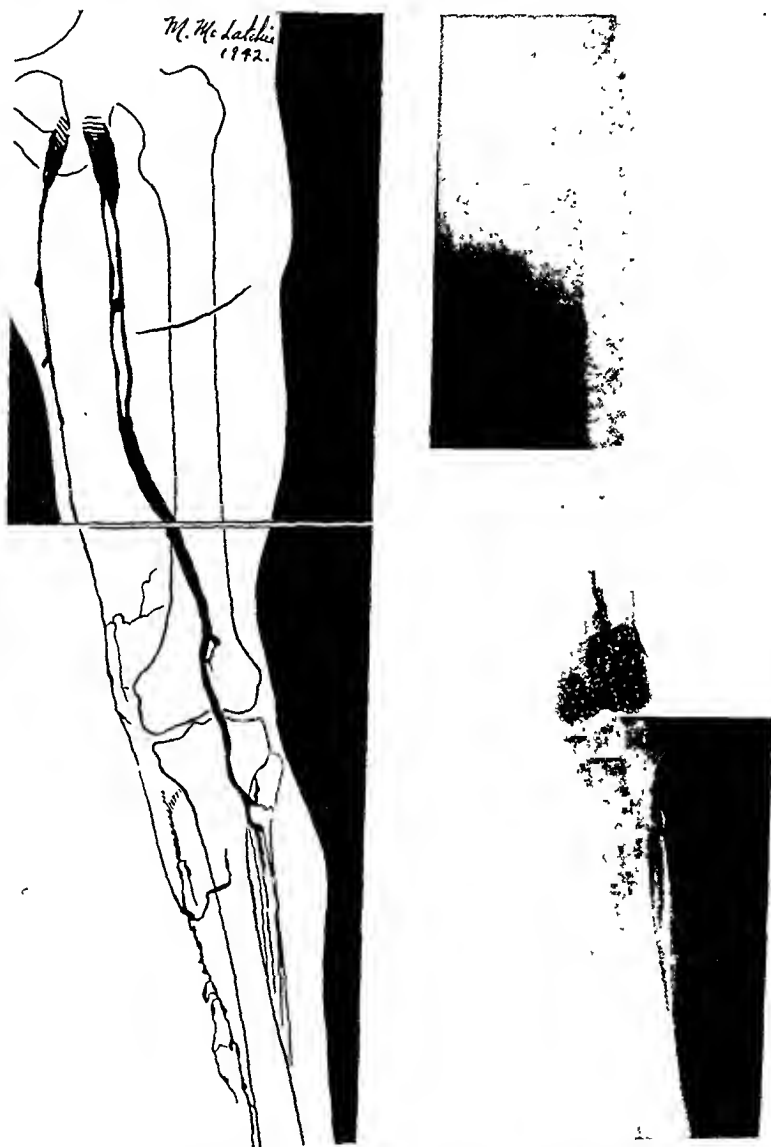


Fig. 11.—A. C. (M. G. H. No. 304502). Mural thrombus seen in the middle and upper portions of the femoral vein. Note deep system filling below.

A. C. (M. G. H. No. 304502), a 56-year-old female, was operated upon Jan. 27, 1942, for a Dupuytren's contracture of the left hand. She was allowed to be out of bed for the first three postoperative days. The following day her temperature rose to 100° F. and twenty-four hours later she developed pleuritic pain over the right chest and a nonproductive cough. Chest x-ray showed a high right diaphragm with linear atelectasis. During the next five days in bed the chest pain disappeared

2. If the superficial femoral vein is thrombosed, the common femoral vein is explored at the level of the sapheno-femoral junction. Proximal and distal thrombi are removed in this order by suction. The femoral and saphenous veins are ligated.

3. If the saphenous vein is varicose in type, and the superficial femoral vein is free of thrombus, the saphenous vein should be ligated at the sapheno-femoral junction and the superficial femoral ligated below the profunda femoris.

B. Type of Ligation.

1. Ligation in continuity should not be done until the surgeon has assured himself, by actually opening the vein, that no thrombus is present at the site of ligation.

2. The vein, thereafter, may either be ligated doubly in continuity, or ligated doubly and divided. The type of suture material must be noted in the record.

REFERENCES

1. Dos Santos, J. C.: Direct Venography: Conception, Technique, First Results, *J. Internat. de chir.* 3: 625, 1938.
2. Bauer, Gunnar: A Venographic Study of Thrombo-Embolie Problems, *Acta chir. Scandinav. (supp. 61)* 84: 1-75, 1940.
3. Dougherty, John, and Homans, John: Venography, A Clinical Study, *Surg., Gynec. & Obst.* 71: 697, 1940.
4. Linton, Robert L.: Personal communications.
5. Hunter, W. C., Sneed, V. D., Robertson, T. D., and Snyder, G. A. C.: Thrombosis of the Deep Veins of the Leg, *Arch. Int. Med.* 68: 1-17, 1941.
6. Fine, Jacob, and Scars, John B.: The Prophylaxis of Pulmonary Embolism by Division of the Femoral Vein, *Ann. Surg.* 114: 801-812, 1941.
7. Welch, C. E., and Faxon, H. H.: Thrombophlebitis and Pulmonary Embolism, *J. A. M. A.* 117: 1502-1508, 1941.

the wound. This very serious complication occurred in both cases when the ligature was placed above a patent profunda femoris. We believe that if the superficial femoral vein had been ligated instead, the venous anastomosis would have been adequate and these catastrophes prevented. Therefore, if the thrombosis in the femoral vein does not extend beyond the mouth of the profunda the superficial femoral vein is chosen for the ligation.

If the long saphenous vein is not thrombosed or varicose in type and it is well delineated by the dye in the phlebogram, it is certain that the ligation can be done below the saphenous vein and usually below the profunda. On the other hand, if the long saphenous vein is involved in the thrombosis, it is necessary to make the incision higher and ligate above the sapheno-femoral junction.

As has been previously emphasized, it is important to open the vein before ligating it, in order to prevent section of a free-lying thrombus by the ligature.

SUMMARY

The members of the Peripheral Vascular Clinic, under Dr. Leland S. McKittrick, have summarized the various procedures indicated in this group of cases for the benefit of the resident staff, who prepare the phlebograms and perform the majority of the ligations. These conclusions are not presented as final dicta, but as a practical guide in the present state of our knowledge.

THERAPY OF THROMBO-EMBOLISM

Patients in whom thrombophlebitis of veins of the lower extremity is suspected or who have had a pulmonary embolus must have the following procedures carried out.

1. Phlebogram: A blood-pressure tourniquet is placed about the mid-calf and inflated to 20 mm. of mercury. 25 c.c. of diodrast is injected into a dorsal vein of the foot or the distal long saphenous vein. The injection should take one minute; exposure is taken at the exact conclusion of the injection.

2. Alternate Method: If, because of sepsis or for other reasons, these veins are not available, the short saphenous vein may be isolated after novocain infiltration behind the external malleolus and injection carried out in a similar fashion.

The manner in which the phlebogram is taken should be noted on the record.

3. The circumference of both legs and thigh at various intervals should be recorded before therapy, and at three-day intervals thereafter. These measurements should be recorded as:

12" above top of patella; 6" above top of patella; 6" below top of patella; 12" below top of patella; maximum lower leg.

4. In addition, the pressure or absence of Homans' sign and of tenderness in the calf should be noted.

It is recommended that venous ligation be done in the following manner:

A. Site.

1. If there is a free superficial femoral vein and the long saphenous vein is not involved and not varicose in type, the ligation is done just below the profunda femoris. This vein is usually found 5 cm. distal to the sapheno-femoral junction.

In no case, however, has there been such degree of spasm as might produce gangrene of the digits, which sometimes happens with thrombosis of the femoral vein where there is an associated spasm of the femoral artery.² A tender cord can be felt on the inner side of the arm over the brachial vein, continuing upward to the axillary vein.

After a period of time ranging from a few days to several weeks, the edema subsides and superficial veins and venules appear over the arm, anterior chest wall, and axilla. The venous pressure is increased and the circulation time prolonged. The veins in the antecubital region do not collapse completely when the arm is held above the heart level. Injection of an opaque dye into the veins about the elbow region reveals new collateral formation, dilatation and distension of veins, irregular course and distribution of the dye through vessels not normally visualized, and evidence of stasis. Photographs taken with infrared technique show numerous superficial veins not normally seen.

Several theories have been advanced for the development of this syndrome. Von Schrotter³ who first described the entity in 1884, maintained that the stretching of the muscle stretched the axillary vein and caused a localized phlebitis resulting in thrombosis. Cadenat⁴ believed that the respiratory effort that was associated with strain distended the vein and produced a change in the intimal lining of the vessel leading to thrombosis. Lowenstein⁵ contended that holding the arm in the abducted position distended the axillary vein and caused the costocoracoid ligament and subclavius muscle to indent it. This distention plus pressure upon the vein was sufficient to produce thrombosis. Gould and Patey⁶ confirmed these findings, but in addition, demonstrated a valve present at the level of the subclavius muscle which ruptured following pressure by the muscle on the axillary vein. This, they advanced as the fundamental cause of the thrombosis. Veal and McFetridge,⁷ on the other hand, held that the thrombosis was due to a compression of the vein below the head of the humerus against the subscapularis muscle. These theories were advanced to explain cases of thrombosis with a history of severe trauma or unusual strain; they do not clarify cases of thrombosis appearing during sleep where there has been no reported trauma or cases where trauma is slight or absent. When thrombosis develops during sleep it is probably caused by a prolonged compression of the vein induced by the position of the arm, particularly when it is elevated over the head or folded under the body. The venous blood flow becomes obstructed and one of two things happens: either the lowered oxygen content of the blood resulting from the obstruction to its flow produces a change in the intimal lining thus forming the basis of the clot, or changes are produced in the constricted region whereby the intima is damaged by direct compression causing thrombosis.⁸

THROMBOSIS OF THE AXILLARY VEIN

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THROMBOSIS of the axillary vein is not a common condition. It is usually associated with indirect trauma in the form of a sprain or strain. The symptoms are identical with thrombophlebitis of the lower extremities except that local and constitutional signs of an inflammatory process are absent. Unlike thrombosis in the lower extremities, it does not follow operations. It is not associated with debilitating conditions nor does it often occur in association with cardiac decompensation. It rarely develops after direct injury to the extremity and rarely complicates blood dyscrasias in which thrombosis are wont to occur.

The literature on the subject is not abundant. Cases are reported occasionally, but no great number by any one observer. The most thorough review of this condition was made by Matas, in 1934, while reporting a case.¹ In his discussion he included diagnosis, pathogenesis, and treatment, as well as medicolegal aspects. However, in reviewing all cases to date one is impressed with the part that trauma plays, varying in degrees from slight to severe. A study of the cases showed the condition to develop in young healthy individuals and to involve the right arm most frequently. When the left arm was involved an undue strain was placed upon it. Males were preponderant in the series but the syndrome was also noted in females. It followed such diverse efforts as those associated with grinding a spark plug, stirring clothes while washing, pulling oneself up by holding on to the head of the bed, checking and restraining a horse, swinging at a golf ball, pitching a baseball, lifting a heavy pressing iron, lifting a cake of ice, lifting a storage battery out of a car, and putting books on a shelf. In rare cases thrombosis developed during sleep without any antecedent history of strain or sprain.

The onset is usually acute but may also be gradual. Pain experienced in the entire arm is followed by swelling and cyanosis which may require several hours or days to develop after the strain. Because of an associated arterial spasm the hand may be colder than that of the uninvolved side and the peripheral pulses may be of smaller volume.

Blood examination revealed a normal cell count and no blood dyscrasias. The blood Wassermann test and chemistry were normal. Venous pressure in the right basilic vein was 130 mm. and in the left 110 mm.

Roentgenograms of the chest failed to reveal evidences of aneurysms or intra-thoracic masses to account for pressure or interference with the return circulation.

Injection of 10 c.c. of diodrast into the cephalic vein showed it to be dilated and tortuous, and to cross over the head of the humerus, continuing in the same pattern over the chest wall. Collaterals were seen in the supraclavicular and cervical regions. A collateral from the cephalic vein crossed the humerus below the neck to empty into the site of the axillary vein. The axillary vein was not visualized and the cephalic vein did not empty into it. A second exposure taken immediately after the first revealed the dye to be present in spots in the cephalic vein. The tortuous vessels over the thoracic cage as well as the collaterals in the supraclavicular and cervical regions were no longer present.



Fig. 1 (Case 1).—Injection of 10 c.c. of diodrast into the cephalic vein reveals the vein to be dilated, tortuous, and continuing in that pattern over the thoracic cage. Collaterals are seen in the supraclavicular and cervical regions. A collateral coming off the cephalic vein crosses the humerus below the neck, emptying into what should be the site of the axillary vein. The cephalic vein per se doesn't empty into the axillary vein.

Comment.—The report just cited is a case of thrombosis of the axillary vein associated with the occupation of hair clipping on horses in which the arm was constantly held in the outstretched and abducted position.

Concerning infection as a causative factor one should note the absence of a temperature rise, both local and general, the absence of the usual history of a chill as is found with thrombosis in the lower extremities, and absence of other evidences of toxemia as well as the presence of a normal blood picture. According to a careful study of the literature there are no blood diseases that predispose to axillary thrombosis.

The role played by the sympathetic nervous system has been emphasized by Cottalorda¹ who believed that the trauma irritated the sympathetic plexus, induced vasospasm and terminated in a vascular lesion. Associated with the venospasm is a thrombosis of the vein which appears clinically as an edema of the arm. Disappearance of the edema and correction of the vasomotor imbalance follow the excision of the involved venous segment.

Similarly, Ochsner and DeBakey² find that vasospasm is a greater factor in producing the clinical manifestations of thrombophlebitis than the thrombus itself.

Thrombosis of the axillary vein should be differentiated from arteriovenous aneurysm. In the former, the oxygen content of the venous blood is low, the temperature of the extremity is normal or subnormal, arterial pulsations are present and are of normal volume, and a thrill and bruit are absent. In the arteriovenous aneurysm the oxygen content of blood from a vein of the extremity is high, the temperature of the extremity is increased, the arterial pulsations are diminished or absent, and a thrill is felt and a bruit heard.

Following herewith are reports of three cases of axillary vein thrombosis, one in a female and two in males, who at the time were in good health with no discernible background to explain the occurrence except trauma.

CASE 1.—S. R., female, aged 62 years, whose occupation was that of clipper of horses' hair, was admitted to the hospital Oct. 7, 1939, because of an enlargement of the right arm and distention of the veins over the right upper extremity, axilla, and pectoral region. This enlargement and distention were of twenty-six years' duration. Patient could not remember any history of acute edema of the arm and claimed to have always been in moderately good health. There was no history of cardiac embarrassment or dyspnea.

General physical examination revealed a well-built and well-nourished female in whom no other findings that could bear on this condition were present. A mild hypertension of 170/90 was found.

The right upper extremity was larger than the left and the veins over the right upper extremity, axilla, and anterior chest wall were dilated, tortuous, and more numerous than those of the left. The veins of the right arm collapsed on elevation but more slowly than of the left. There were no evidences of palmar ischemia on elevation nor of dependent rubor. The brachial, radial, and ulnar arteries of both extremities were of equal volume and the temperature of both extremities the same. No cord or thrill could be felt in the axilla, nor was a bruit heard.

Comparative measurements were as follows.

	RIGHT	LEFT	DIFFERENCE
Junction of humerus and shoulder	28½ cm.	30½ cm.	2 cm.
Mid humeral	28½ cm.	30 cm.	1½ cm.
Elbow	25½ cm.	26 cm.	½ cm.
Mid forearm	26 cm.	26¾ cm.	¾ cm.
Wrist	17¾ cm.	18 cm.	¼ cm.
Palm	20½ cm.	21 cm.	½ cm.



Fig 2 (Case 3) —Infrared photography reveals numerous superficial veins in the left axilla and on the under surface of the upper arm

Upon elevation of both extremities above the heart level the veins of the right upper extremity collapsed readily, whereas those of the left were slow, some not collapsing at all. The arterial circulation was not impaired, the oscillometric reading over the left brachial artery being seven, and over the right, nine. This difference was probably due to a spasm associated with the venous thrombosis. The left hand was colder than the right. Circulation time with calcium gluconate was twenty one seconds as compared with a normal of ten to twelve seconds. Venous pressure was 410 mm. of water as compared with a normal of 60 to 120 mm.

CASE 2.—P. B., a white male, aged 23 years, helper on a truck, on June 7, 1939, lifted a case of milk weighing sixty pounds from a platform onto a truck. As he lifted the case he felt a sudden pain in the left arm. The arm subsequently became stiff and swollen. Within four hours the entire left upper extremity became so swollen that he had to support it with his right hand. Several days later, as the swelling decreased, he noticed numerous prominent veins over the arm. The hand was heavy and discolored.

Examination Aug. 29, 1939, revealed a well-nourished male in whom all physical findings were negative. The laboratory data bore no significant relation to the local condition. The veins over the left upper extremity in the axilla and over the chest wall were more numerous and dilated than those on the right side. The veins in the left antecubital region collapsed more slowly on elevation above the heart level than did those on the right. The brachial, radial, and ulnar pulsations could be felt and were of good volume. There was no bruit or thrill. The left hand was slightly colder than the right and the hand grasp, weaker. A tender cord was present in the axilla.

The left arm was larger than the right, the exact comparative measurements being as follows:

	RIGHT	LEFT	DIFFERENCE
Junction of shoulder and arm	31 cm.	32 cm.	1 cm.
Mid-arm	27 cm.	28 cm.	1 cm.
Elbow	24½ cm.	26½ cm.	2 cm.
Wrist	16½ cm.	18 cm.	1½ cm.

Circulation time using 10 per cent calcium gluconate was computed at twenty-five seconds in the left arm and ten seconds in the right. The venous pressure in the left basilic vein was 210 mm. of water as compared with 90 mm. of water in the right basilic vein.

Radiographs of the left shoulder region failed to reveal any evidence of bone or joint pathology and radiographs of the thoracic cage revealed no evidence of tumor or masses.

Treatment consisted of the application of an elastic bandage spirally from the palm up to the axilla, enabling the patient to resume his duties.

Re-examination three months later revealed the left upper extremity still larger than the right. The veins had not receded in size or number. The mass in the axilla, previously tender, was no longer felt. The antecubital veins still collapsed slowly upon elevation.

Comment.—The case described is one of axillary vein thrombosis which followed a severe and sudden sprain associated with the lifting of a weight of sixty pounds.

CASE 3.—J. K., a white male, aged 27 years, employed as a shipping clerk, on March 10, 1939, pulled and pushed a silk-measuring machine weighing 250 300 pounds. He felt a sudden shock-like pain in the left arm. About one-half hour later the hand became swollen and blue. A day later the entire left upper extremity became swollen and hard and a painful mass was felt in the axilla.

Examination March 26, 1939, revealed the left upper extremity enlarged and of a dusky discoloration with numerous superficial veins and venules over the left arm, left anterior pectoral and axillary regions. The lateral thoracic vein was prominent. Veins in the elbow as well as those on the dorsum of the left hand were very distended. There was no clubbing of the fingers and motion in the joints was unimpaired. A tender cord was felt in the left axilla.

circulation established. Following prolonged use, the patient may feel a sense of heaviness, fullness, fatigue, or cramps in the extremity. In some cases there may be recurrence of the edema following exertion. No deaths from embolism have been reported.

SUMMARY

1. Three cases of axillary vein thrombosis have been described, one in a female in which the right arm was involved and two in males in whom the left arm was involved.
2. The theories as to its formation have been reviewed briefly.
3. The findings helpful in diagnosis have been enumerated.
4. A brief résumé of the treatment and prognosis has also been included.

REFERENCES

1. Matas, R.: Primary Thrombosis of the Axillary Vein Caused by Strain, *Am. J. Surg.* 24: 642-666, 1934.
2. Uggeri, C., and Massone, A.: La sintomatologia Arteriale delle flebiti degli arti (The Arterial Symptomatology of Phlebitis of the Extremities), *Arch. ital. di chir.* 49: 429, 1938 abstracted in *Surg., Gynec. & Obst.* 68: 533, 1939.
3. von Schrotter: In Nothnagel, *Handbuch der Pathologie und Therapie*, Vienna, 1901, Alfred Holder, 15/13: 533.
4. Cadenat, F. M.: Les Thrombophlebitis du membre superieure, *Paris méd.* 35: 253-259, 1920.
5. Lowenstein, P. S.: Thrombosis of the Axillary Vein: An Anatomic Study, *J. A. M. A.* 82: 854-857, 1924.
6. Gould, E. P., and Patey, D. H.: Primary Thrombosis of the Axillary Vein, *Brit. J. Surg.* 16: 208-213, 1928.
7. Veal, J. R., and McFetridge, E. M.: Primary Thrombosis of the Axillary Vein, *Arch. Surg.* 31: 271-289, 1935.
8. Veal, J. R.: Thrombosis of the Axillary and Subclavian Veins, *Am. J. M. Sc.* 200: 27-29, 1940.
9. Ochsner, A., and DeBakey, M.: Thrombophlebitis: The Role of Vasospasm in the Production of the Clinical Manifestations, *J. A. M. A.* 114: 117-125, 1940.
10. Ochsner, A., and DeBakey, M.: Treatment of Thrombophlebitis by Novocain Block of Sympathetics, *Am. J. Surg.* 5: 491-497, 1939.

X-rays of the thoracic cage failed to reveal any evidence of masses or growths to account for obstruction. Infra-red photographs showed numerous superficial veins over the left arm and in the left axilla.

Re-examination June 14, 1939, revealed the left upper extremity still enlarged and of a dusky discoloration. There was no restriction in mobility of the joints. The venous pattern previously described had not changed. The cord in the axilla which was tender when first examined was still present, although no longer tender. Circulation time was still twenty-one seconds and venous pressure had decreased from 410 mm. to 380 mm. of water.

Subsequent examinations revealed the extremity still enlarged with the veins distended.

Comment.—The above is a case of thrombosis of the axillary vein following the undue strain of pushing and pulling a 250-300 pound machine.

DIAGNOSIS

A diagnosis of thrombosis of the axillary vein can be made from (1) a history of trauma which may vary in intensity from slight to severe, (2) swelling and enlargement of the extremity, (3) prominence of the existing veins and appearance of new collateral veins and venules, (4) distension and failure of the veins to collapse completely and readily when the extremity is elevated above the heart level, (5) increase in the circulation time, (6) increase in the venous pressure, (7) visualization by means of the injection of an opaque medium of new collaterals, dilatation and distension of veins, and stasis, (8) increase in the number of superficial veins as shown in photographs taken with infra-red technique.

TREATMENT

The traditional treatment for axillary thrombosis in the acute stage is rest to the part, elevation, and local application of hot, moist packs. When the edema subsides, an Ace bandage extending spirally from palm to shoulder is applied until a new collateral circulation develops.

On the basis of the part played by the sympathetic nervous system in thrombophlebitis, however, Ochsner and DeBakey¹⁰ advocate the infiltration of novocain or procaine into the corresponding lumbar and cervicodorsal sympathetic ganglia. They have used this method with success in cases of thrombophlebitis of the extremities, complete relief from pain and disappearance of the edema having followed interruption of the sympathetic reflexes. This form of therapy avoids the drastic approach of Cottalorda,¹ namely thrombectomy and excision of the affected segment, and thus has the obvious advantages of conservative treatment.

Activity is resumed gradually with the possibility of recurrence kept in mind.

PROGNOSIS

The duration of the edema and swelling is variable and severity of the residual symptoms depends on the extent of the new collateral venous

man of shyness and of self-effacing modesty he would not wish to have either his personality or his achievements discussed, much less praised. He must not mind, however, if we say that he was one of the last of that group of men in American medicine who gave us our national medical character and who brought to it the initiative, honesty, and originality of the pioneer and contributed vastly to the collective knowledge of today.

A master surgeon of all time, his interests were manifold but he was truly a pioneer in joining to the anatomie and pathologic aspects of surgery an interest in the physiologic. In emphasizing this point I will attempt to discuss a subject that might well have interested him, since it deals with the well-being of the sick, that is, some of the abnormal chemical changes encountered in surgical patients.

A complete review of the historical side of this subject would necessitate reference to much of the basic work in chemistry and physiology, which is clearly impossible, but a few of the landmarks may be mentioned. Sanctorius Sanctorius,³² the "first famous master of experimental medicine," published his *Ars de Statica Medicina*, in 1614, in which he tells of his observations with the thermometer, pulsilogium, and the balance. His aphorisms dealing with insensible perspiration are of particular interest since the phrase is his. In Aphorism II he states, "If a physician who has the care of another's health is acquainted only with the sensible supplies and evacuations and knows nothing of the waste that is daily made by insensible perspiration, he will only deceive his patient and never cure him."

Other men studied insensible perspiration, one of the most interesting of whom was Dr. John Lining of Charleston, South Carolina, who throughout all seasons of the year 1740, carried on observations on himself concerning loss of weight through perspiration. He hoped that these studies made in a climate subject to violent changes might throw light on "the nature and predisponent causes of epidemic diseases."

Many studies of insensible perspiration have been made since, particularly by Lavoisier, who demarked cutaneous respiration from pulmonary respiration up to the definitive investigations of Benedict and Root,³ in 1926, that showed that the insensible loss varies with the rate of metabolism.

We now know that the maintenance of water and electrolyte content of the body is important but it is interesting to read the short communication written to the London Medical Gazette, in 1831, by Dr. W. B. O'Shaughnessy of Newcastle-on-Tyne about his observations on patients with cholera.²⁷ In it he stated:

1. The blood drawn in the worst cases of the cholera is unchanged in its anatomical or globular structure.
2. It has lost a large proportion of its water, 1,000 parts of cholera serum having but the average of 850 parts of water.
3. It has lost also a great proportion of its neutral saline ingredients.

A REVIEW OF STUDIES ON WATER AND ELECTROLYTE BALANCE IN SURGICAL PATIENTS

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THE chief characteristic of medicine in this country has always been originality of thought combined with a sturdy independence of action. It may have been a fortunate deprivation that there were no medical schools here for more than one hundred and fifty years after the first settlements were established. Such medical schools as existed abroad were shackled by ropes of convention and bonds of authority while in this new country the sick were treated by men brought up in the apprentice system where academic fixation was lacking and initiative was untrammelled. Only five medical schools had been established before 1800, designed to supplement the apprentice system of training but accomplishing it in a formal, sterile manner. By this time the great migration of population to the west was well under way, to continue for more than a century. With the waves of pioneers went their doctors, who worked alone, without opportunity for consultation or formalized study. These men were forced to solve the many problems of practice through their own ingenuity and originality.

It was in this environment and because of it that American medicine first began to make significant additions to medical progress. McDowell, Beaumont, Crawford, Sims, Drake and others made their contributions under these circumstances of isolation, with freedom for unorthodox and unfettered activity. With the mass movement of people to the West came a corresponding expansion of medicine. Literally hundreds of medical schools were established, most of them without facilities but the right to collect fees and to grant diplomas. A majority of the graduates of these schools were better than the sources of their training, and medicine improved through the impetus of men rather than from that of their schools. We are familiar with the sweeping changes that have taken place in medical education in the last generation. Medical schools have assumed university stature and have become centers for the nurture of genius and of intellectual curiosity. Medicine has now become co-operative while still fostering individualism.

We have met tonight to honor one of the last of the group of pioneer individualists who bridged the gap from the old to the new.

The last of the many important contributions of the frontier physician to medicine was the development of the idea of cooperative practice in the small Minnesota town where Edward Starr Judd lived and worked. A

this observation being confirmed by Cooke, Rodenbaugh, and Whipple, in 1916. In 1918, McCann described the alkalosis which occurs from loss of stomach secretions associated with pyloric obstruction. In 1920, MacCallum and his associates described the fall in plasma chloride concentration after the pylorus was obstructed. They also showed that the giving of sodium chloride prevented both the fall in plasma chlorides and the rise in the carbon dioxide combining power of the plasma, and that the administration of either hydrochloric acid or sodium bicarbonate prevented neither. Haden and Orr, in a series of important studies on the altered chemistry associated with intestinal obstruction, emphasized that azotemia, hypochloremia and alkalosis are present in high intestinal obstruction. They corroborated the findings of Hartwell and Hoguet on the beneficial effects of the giving of saline solution and demonstrated that many salts of sodium, and of chlorine other than sodium chloride, may be ineffective. They showed that water alone does not prevent the onset of symptoms and death from high intestinal obstruction as had been postulated by Hartwell and Hoguet. Many investigators in the laboratory and the ward have substantiated and continued these studies and one can only mention the names of a few for lack of space. Important and basic contributions have been made by Gamble, Gatch, Hartmann, Peters, Darrow, and many others to put this whole aspect of disease upon firm scientific foundations.

From this accumulated knowledge built up by many investigators it has become clear to the clinician that the deprivation of, or loss of, water and electrolytes from the body through disease or treatment will give rise to untoward symptoms and may be the cause of death. Physicians have long recognized the truth of these observations and fluids of many sorts have been given to sick patients in many ways.

Some years ago it was clear to us that in our surgical wards we were giving fluids to patients in a more or less haphazard way and we began to study these problems in a quantitative manner in the hope that we might develop facts that would enable us to have simpler working rules for the accurate replacement of water and electrolytes when they were needed. I propose to give a brief summary of the various studies made over the past eight years, knowing, however, that many of you are already all too familiar with them.

The animal life of the ocean that adopted a terrestrial life could not free itself from the sea and therefore had to carry the sea with it as extracellular fluid. As a consequence, it added the tremendous task of maintaining the constancy of that infinitesimal portion of the ocean that it contained within its corporeal limits to the already highly complex task of regulating internal environment. This task is more or less successfully performed by the normal animal with the adaption of varied and more or less efficient physiologic expedients, principally the skin and glomeruli.

4. Of the free alkali contained in healthy serum, not a particle is present in some cholera cases, and barely a trace in others.

5. Urea exists in the cases where suppression of urine has been a marked symptom.

6. All the salts deficient in the blood, especially the alkali or carbonate of soda, are present in large quantities in the peculiar white dejected matters.

He then states that cure is seemingly dependent upon two principles: "First, to restore the blood to its natural specific growth (i.e. its water content); second, to restore its deficient saline matters." He goes on to state that "the first of these can only be effected by absorption, by imbibition, or by the injection of aqueous fluid into the veins. The same remarks with sufficiently obvious modifications, apply to the second." He recommends for practical therapy, "in severer cases, copious enemata of warm water, holding the natural salts of the blood in solution. . . . When absorption is entirely suspended, the author recommends the injection into the veins of tepid water holding a solution of the normal salts of the blood." These brilliant observations carried on 110 years ago with meager facilities and methods show clearly that dehydration and salt depletion are serious factors in cholera.

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The use of salt solutions received its real impetus after the reports by Rogers, and Nichols and Andrews in 1909, of its efficacy as therapy in the treatment of cholera during an epidemic of that disease in the Philippine Islands. The use of saline solution in surgery was slowly adopted. At first it was usually given as a retention enema. Later it was given as a rectal drip after the popularization of this method by J. B. Murphy. In 1912, Hartwell and Hognet showed that, after complete obstruction of the lower duodenum in animals, life could be greatly prolonged by the daily subcutaneous administration of normal salt solution in amounts slightly in excess of the total volume of the urine and vomitus of the previous twenty-four-hour period. They concluded that the effect was due to a relief of dehydration usually present to a marked degree in high intestinal obstruction.

In 1914, Tileston and Comfort observed the rise in blood nonprotein nitrogen that accompanies the dehydration of high intestinal obstruction,

this observation being confirmed by Cooke, Rodenbaugh, and Whipple, in 1916. In 1918, McCann described the alkalosis which occurs from loss of stomach secretions associated with pyloric obstruction. In 1920, MacCallum and his associates described the fall in plasma chloride concentration after the pylorus was obstructed. They also showed that the giving of sodium chloride prevented both the fall in plasma chlorides and the rise in the carbon dioxide combining power of the plasma, and that the administration of either hydrochloric acid or sodium bicarbonate prevented neither. Haden and Orr, in a series of important studies on the altered chemistry associated with intestinal obstruction, emphasized that azotemia, hypochloremia and alkalosis are present in high intestinal obstruction. They corroborated the findings of Hartwell and Hoguet on the beneficial effects of the giving of saline solution and demonstrated that many salts of sodium, and of chlorine other than sodium chloride, may be ineffective. They showed that water alone does not prevent the onset of symptoms and death from high intestinal obstruction as had been postulated by Hartwell and Hoguet. Many investigators in the laboratory and the ward have substantiated and continued these studies and one can only mention the names of a few for lack of space. Important and basic contributions have been made by Gamble, Gateh, Hartmann, Peters, Darrow, and many others to put this whole aspect of disease upon firm scientific foundations.

From this accumulated knowledge built up by many investigators it has become clear to the clinician that the deprivation of, or loss of, water and electrolytes from the body through disease or treatment will give rise to untoward symptoms and may be the cause of death. Physicians have long recognized the truth of these observations and fluids of many sorts have been given to sick patients in many ways.

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creases;^{3, 5, 25} allowance, therefore, should be approximately made. From direct determinations on surgical patients it was concluded that the insensible loss could usually be covered by 1,000 c.c. in small inactive individuals and by 1,500 c.c. in the larger or more active.⁶ The water necessary to excrete the average amount of waste formed in the body daily (35 Gm.) amounts to about 500 c.c. of water with the normal kidney concentrating near capacity (specific gravity, 1.030).¹⁶ The insufficient kidney requires more water to excrete 35 Gm. of waste, therefore, to have an adequate margin of safety requires that 1,000 c.c. be considered the minimum urine excretion in the surgical patient.⁶ The water lost normally in the stool is small, 100 c.c. daily; that lost by sweating varies with the season, the temperature of the operating room, the extent of draping, and the type of covering of the individual before full reaction from the anesthesia has occurred. During the hot, humid weather of a Michigan summer, without air conditioning either in the ward or operating room, as much as 4,000 c.c. of sweat was lost in a single twenty-four-hour period by a patient quietly lying in bed.³⁶ It was concluded, therefore, that an uncomplicated surgical case, not perspiring, requires from 2,000 to 2,500 c.c. of water daily. Due allowance must be made from the increased requirements incident to fever, hyperthyroidism, and sweating. In general, under these conditions 3,000 to 3,500 c.c. are required.⁶

Beside the water needed to keep the body water within normal limits of composition and amount, provision must be made for the replacement of the salts lost. In contrast with the relatively large amounts of water that must be excreted daily, the body is capable of conserving certain electrolytes when the intake is insufficient so that a normal nonsweating person will excrete only traces of chloride in the urine^{2, 22} (0.1 Gm. per twenty-four hours)⁶ when there is no excess intake. The administration of 5 Gm. of salt therefore provides more than adequately for normal needs.⁶ The concentration of salt in sweat varies widely in different individuals and in the same person with season, state of training, amount of sweat, and possibly with the blood chloride level.⁹ It is, therefore, impossible to approximate, without elaborate studies, the salt lost through sweating. It is suggested that during the hot humid days of summer a minimum of 10 Gm. of salt be provided daily either orally or parenterally. If this amount is in excess of that needed the kidney will excrete it. The abnormal losses of water and electrolytes through fistulas, Wangensteen drainage, bile drainage, vomiting, and diarrhea are readily balanced by the parenteral replacement with an equal volume of normal saline or Ringer's solution.¹⁹

The problem of correcting the dehydration and electrolyte imbalance that is frequently present when the patient first consults a physician is not as simple as is the prevention of dehydration and electrolyte imbalance during hospitalization. Simple dehydration (water deprivation

The human being in the light of comparative physiologic knowledge is in some ways inferior to many of the so-called lower forms of life. Especially is this true in his relative lack of safeguards for the maintenance of the constancy of body fluids under adverse environmental conditions. For instance, during hot weather, man regulates his body temperature by excreting as sweat, a dilute salt solution, yet he experiences no salt hunger even though the loss of salt may cause his death. However, the dog, the ass, and the ox under like circumstances are spared a similar fate; the dog and the ass⁹ because they do not lose salt in significant quantities with the water vaporized, the ox because, although he sweats a weak salt solution, develops salt hunger as the sodium chloride of the body is depleted and will therefore make a supreme effort to get the needed salt. The physiologist knowing only the working of the heat regulating mechanisms of the ass could die of salt depletion from sweating, drinking water and swearing until the end that he could not be dying of lack of salt because the amount of salt lost in sweat was insignificant; and he who knew only the physiology of the ox would die with the salt before him while he awaited the sensation of salt hunger to urge him to take it. It is therefore obvious that the ultimate basis for the establishment of practical principles for regulating the salt and fluid balance of an ill man must come from experimental work done on man. Furthermore, it would be likewise hazardous to set up those principles upon the basis of knowledge gained from acute experiments on normal man because the basic fluid and salt requirements are affected, for instance, by the metabolic rate,^{3, 24} the blood and lymph loss during the operation, the rate of loss in exudates, and through the enteric, biliary, pancreatic, and lymphatic fistulae. Therefore, it was realized that although a great mass of knowledge concerning salt and water metabolism was available it could not be intelligently employed in surgery until the specific requirements of man suffering the varied ills that are treated surgically were known. It has been largely toward that end that the major part of the work done on water and salt balance at the University of Michigan has been directed.

It was realized when the problem was first undertaken that a basic approach to the problem required that the water needs of the surgical patient be known; that necessitated the establishment of the amounts of water and salt required by the relatively normal individual under the conditions to which a patient would be subjected during and after a surgical procedure. The factors that had to be taken into account were insensible loss of water, the water necessary to excrete body wastes without having the kidney concentrate the urine to its limit of capacity, the water lost in stool, and the water lost by sweating. The insensible loss of water from skin and lungs amounts in the average adult to about 1,200 c.c. each twenty-four hours.³ This amount increases as metabolic rate increases and as breathing in-

Simple water deficiency and simple electrolyte deficiency although seen as separate entities are very commonly combined.²³ It is obvious from the preceding discussion that a fairly objective clinical approach to the correction of both conditions when in combination may be provided without recourse to laboratory determinations. This is of importance to the general practitioner who does not have ready access to a clinical laboratory and it will become more important in the larger clinics as the labor and monetary shortage imposed by war become more acute.

Since thirst indicates the lack of water in both extracellular and cellular compartments (simple dehydration), its alleviation first with glucose solution (5 to 10 per cent)³⁸ will correct the simple dehydration. Subsequently, normal saline or Ringer's solution, to which glucose may be added, should be continued at the rate of 200 to 300 c.c. per hour until the signs and symptoms of shock are alleviated. That is, the blood pressure rise and the pulse rate fall reach a plateau, the extremities become warm, the superficial veins fill at approximately the normal rate when occluded, and weakness and apathy diminish in intensity. It is obvious that should the serum proteins be low, complete restoration of blood volume to normal with saline solution should not be expected. In practice, therefore, after 3,000 to 4,000 c.c. of saline solution have been given, hemoglobin and red cell determinations should be made. Should the hemoglobin be below 70 or the red blood cell count be below 3,000,000 it is likely that the serum proteins are low, especially if malnutrition is present or blood loss has occurred. In such a case maximum improvement cannot be expected until blood or plasma has been given in addition to the salt solution. After the initial correction of the dehydration and electrolyte imbalance the principles of volume-for-volume replacement plus 5 Gm. of extra salt daily to provide a slight excess, and the maintenance of a urine volume above 1,000 c.c. will generally serve as adequate guides for subsequent management.

It must be realized that the administration of salt in amounts in excess of those actually required is not without danger, especially in sick individuals. The retention of salt and water results ultimately in edema when the amount of excess salt is less than that which results in significant retention in the normal individual.^{1, 6, 19, 20, 37} The dangers of edema developing in a sick surgical patient have been well shown. It is, therefore, highly desirable, especially in the very ill patient, to provide water and salt in amounts as near the physiologic needs of the individual as possible if we do not wish to act as a drag on nature in her attempts to heal.

REFERENCES

1. Baird, M. M., and Haldane, J. B. S.: *J. Physiol.* 56: 259, 1922.
2. Benedict, F. G.: *Carnegie Inst. Wash. Year Book* 203: 268, 1915.
3. Benedict, F. G., and Root, H. F.: *Arch. Int. Med.* 38: 1, 1926.
1. Collier, F. A., and Maddock, W. G.: *Ann. Surg.* 98: 952, 1933.

without electrolyte loss) such as occurs with obstruction of the esophagus and is manifested by thirst, dry mucous membranes, and oliguria is very easily correctable with glucose solution. Salt solution, if given, will not allay the thirst. The situation and consequences are somewhat analogous to the thirsty shipwrecked mariner given sea water to drink. The allaying of thirst and the raising of the twenty-four-hour urine volume above 1,000 c.c. serve as indications that enough glucose solution has been given to a person suffering simple dehydration.

The patient suffering from electrolyte deficiency (diarrhea, fistulas, Addison's disease, profuse sweating), since he is usually able to satisfy his thirst if water is available, experiences neither salt hunger nor thirst even though his extracellular fluid volume (blood volume included) be so reduced that he lies in deep shock.^{11, 23, 35} Blood examination shows a high hematocrit, and a high serum protein concentration provided that a normal red blood cell and protein content were present before the electrolyte loss. Chloride and sodium are decreased in the plasma. If the loss of chloride exceeds the loss of base (vomiting, exclusive of achlorhydria) the blood chloride level is more rapidly diminished than is the base.¹¹ If base loss should balance the chloride loss (vomiting with achlorhydria), or exceed it (biliary or pancreatic fistula), the blood chloride level falls relatively more slowly. In any case, since extracellular fluid volume as influenced by its ionic constituents changes mainly with alterations in its total base content,²⁸ it is obvious that the blood chloride level is not sufficient to evaluate the severity or the cause of the dehydration in the various gastrointestinal pathologic states. However, as Peters and Van Slyke²⁹ have stated, the determination of the HCO_3 of the blood together with the determination of chloride would provide a basis for estimating the concentration of base and, as a consequence, a more objective determination of the severity of the dehydration. It is presumed that herein lies the explanation for the occasional difficulty that we have experienced with electrolyte and water replacement when it is universally attempted upon the basis of blood chloride level alone.³⁰

Neither do the hematocrit or the serum protein levels serve as an adequate measure of extracellular fluid volume replacement as they are too variable, especially in the pathologic states with which electrolyte imbalance occurs. Consequently, in cases characterized by a primary electrolyte deficiency that show the signs and suffer the symptoms of shock, as a consequence of the decreased blood volume, the alleviation of symptoms and disappearance of the signs of shock, and the maintenance of a satisfactory urine volume constitute an adequate basis for judging the adequacy of the electrolyte and water replacement without recourse to laboratory determination of blood chloride and bicarbonate levels. However, it is hoped that work now in progress in many laboratories may soon enable us to employ more scientific means in the control of electrolyte replacement therapy.

A MODIFIED WHIPPLE OPERATION FOR CARCINOMA OF THE HEAD OF THE PANCREAS*

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SINCE the demonstration by Whipple, Parsons, and Mullins, in 1935, that ligation of the pancreatic duct could usually be tolerated in the course of partial pancreatectomy for carcinoma of the ampulla of Vater in man, renewed interest has been aroused in radical surgical approaches to the pancreas. This trend was strengthened by Whipple's report, in 1938, of successful extirpation of carcinoma of the head of the pancreas. Prior to 1941, procedures designed for extirpation of such lesions were in general performed in two stages. One such procedure was successfully carried out by Dr. John R. Paine at this clinic. The patient survived for three months after the second stage operation and died elsewhere of unknown cause, an autopsy not being obtained.

With the advent of vitamin K and more adequate use of blood and plasma transfusions, however, the trend is now toward a one-stage operation. In November, 1941, Trimble, Parsons, and Sherman reported a successful one-stage procedure, the technique being essentially the same as that now in use by Whipple. In this procedure, partial gastrectomy with an anterior Polya gastrojejunostomy was performed, the common bile duct being implanted into the jejunum just distal to the gastric stoma.

Upon review of the pertinent literature, several considerations become apparent with regard to the performance of a satisfactory operation. The first of these is the prevention of ascending cholangitis following anastomosis between the biliary and intestinal tracts, a complication of considerable frequency in the best of hands. Trautmann, Robbins, and Stewart showed in experimental studies in dogs that simple side-to-side anastomosis of bowel to gall bladder uniformly is followed by passage of intestinal content into the biliary tract. Wangenstein concluded that even though this occurs, the essential factor in preventing cholangitis and hepatitis is the prevention of obstruction at the stoma. Bachrach and Fogelson confirmed this in the case of choledochojejunostomy.

Various authors have described procedures intended to prevent reverse flow into the biliary tract. Kausch described a Y procedure somewhat similar to the Roux gastrojejunal anastomosis, and others have offered

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5. Coller, F. A., and Maddock, W. G.: West. J. Surg. 41: 438, 1933.
6. Coller, F. A., and Maddock, W. G.: Surg. Gynec. & Obst. 70: 340, 1940.
7. Cooke, J. V., Rodenbaugh, F. H., and Whipple, G. H.: J. Exper. Med. 23: 717, 1916.
8. Darrow, D. C., and Yannet, H.: J. Clin. Investigation 15: 419, 1936.
9. Dill, D. B.: Life, Heat and Altitude, Cambridge, Mass., 1938, Harvard University Press.
10. Gamble, J. L., and Ross, S. G.: J. Clin. Investigation 1: 403, 1925.
11. Gamble, J. L., and McIver, M. A.: J. Exper. Med. 48: 859, 1928.
12. Gateh, W. D., Trusler, H. W., and Ayers, K. D.: Am. J. M. Sc. 173: 649, 1927.
13. Haden, R. L., and Orr, T. G.: J. A. M. A. 82: 1515, 1924.
14. Hartwell, J. A., and Hogue, J. P.: J. A. M. A. 59: 82, 1912.
15. Hartmann, A. F.: J. A. M. A. 103: 1349, 1934.
16. Lashmet, F. H., and Newburgh, L. H.: J. Clin. Investigation 11: 1003, 1932.
17. Lining, John: Phil. Tr. 42: 491, 1742-43; 43: 318, 1744-45.
18. MacCallum, W. G., Lintz, J., Vermilye, H. N., Leggett, T. H., and Boas, E.: Bull. Johns Hopkins Hosp. 31: 1, 1920.
19. Maddock, W. G., and Coller, F. A.: J. A. M. A. 108: 1, 1937.
20. Matas, R.: Ann. Surg. 79: 643, 1924.
21. McCann, W. S.: J. Biol. Chem. 35: 553, 1918.
22. McLean, F. C.: J. Exper. Med. 22: 212, 1915.
23. Nadal, J. W., Pedersen, S., and Maddock, W. G.: J. Clin. Investigation 20: 691, 1941.
24. Newburgh, L. H., Wiley, F. H., and Lashmet, F. H.: J. Clin. Investigation 10: 703, 1931.
25. Newburgh, L. H., Johnston, M. W., Lashmet, F. H., and Sheldon, J. M.: J. Nutrition 13: 203, 1937.
26. Nichols, H. J., and Andrews, V. L.: Philippine J. Sc. 4: 81, 1909.
27. O'Shaughnessy, W. B.: Letter to London Medical Gazette 9: 486, 1831-1832.
28. Peters, J. P.: Body Water, Springfield, Ill., 1935, Charles C Thomas, Publisher.
29. Peters, J. P., and van Slyke, D. D.: Quantitative Clinical Chemistry, vol. I, Baltimore, 1937, Williams & Wilkins Company, p. 778.
30. Power, F. H., Pedersen, S., and Maddock, W. G.: J. Pediat. 18: 776, 1941.
31. Rogers, L.: Cholera and Its Treatment, London, 1913, Oxford University Press.
32. Sanctorius, S.: Ars Sanctorii Sanctorii, De statica medicina, aphorismorum sectionibus septem comprehensi. Accedit staticomostix sive ejusdem artis demolitio, Venec, 1614, Hippolyti Obicci.
33. Tileston, W., and Comfort, C. W.: Arch. Int. Med. 14: 620, 1914.
34. Schmidt, Karl: Charakteristik der epidemischen Cholera gegenüber verwandten Transudationsanomalien. Eine physiologische-chemische Untersuchung. Leipzig u. Mitau, 1850.
35. Talbot, J. H., and Mickelsen, J.: J. Clin. Investigation 12: 533, 1933.
36. Wassel, G. K.: Univ. Hosp. Bull. Ann Arbor 4: 26, 1938.
37. White, J. C., Sweet, W. H., and Hurwitt, E. S.: Ann. Surg. 107: 438, 1938.
38. Winslow, S. B., SURGERY 4: 867, 1938.

superior mesenteric artery and vein were identified and followed upward, and were found to pass very close to the left lateral margin of the tumor. Nevertheless, it was possible to cut across the head of the pancreas, sparing these vessels. The main duct was tied with silk of five-pound test. The common bile duct was tied with heavy silk and divided near the duodenum. The posterior capsule of the pancreas was sutured to the anterior with mattress sutures of five-pound test silk. At this point it became apparent that the circulation to the last part of the duodenum

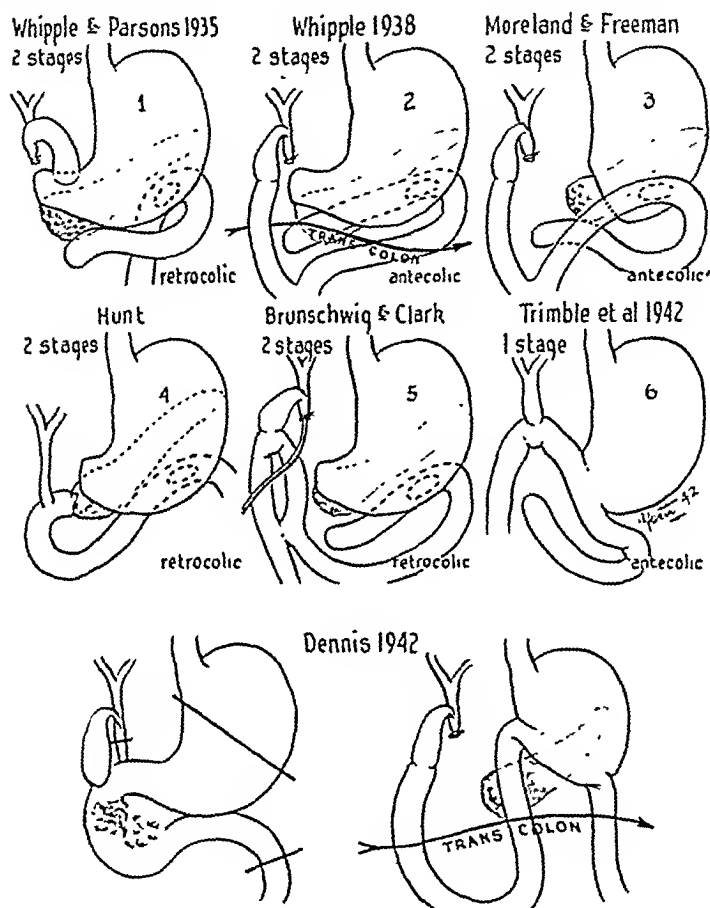


Fig 1.—Outline diagrams of several operative procedures which have been employed for extirpation of carcinoma of either the ampulla of Vater or of the head of the pancreas.

and to the lowest third of the stomach was inadequate, and both were, therefore, resected, the lines of section crossing the stomach in the midportion, and the jejunum about eight inches below the ligament of Treitz. The gall bladder, which had been found tensely distended, was emptied without spillage by trocar, the remaining end of the jejunum was brought retrocolically through the channel formerly occupied by the duodenum, and an end-to-end cholecystojejunostomy was performed by a closed technique similar to that of Martzloff and Burget, with fine catgut internally and silk mattress sutures externally, a few grains of sulfathiazole being placed between the rows of sutures. Leaving a long (40 cm.) proximal loop, and implanting

modifications, all, however, with short segments separating the biliary anastomosis from the main enteric stream.

A further consideration is the development of the simplest procedure possible, one with a minimum of anastomoses, etc., a factor demanded by the usual poor condition of these patients. Finally, leakage of pancreatic juice into tissues or suture lines must be prevented. (Verne C. Hunt has reported successful implantation of the pancreas into the end of the jejunum, and T. G. Orr has also had two successful cases.)

I have operated upon a case by a variant of these procedures which seems to overcome the difficulties outlined above. A wide stoma is assured by end-to-end cholecystojejunostomy; regurgitation into the biliary tract is minimized by use of a long jejunal segment separating the biliary from the gastric anastomosis. There are but two anastomoses, and pancreatic digestion is rendered unlikely by adequate use of drainage.

CASE REPORT

History.—H. V. J. (U. H. No. 715130), a man of 64, was admitted on the medical service Dec. 18, 1941, with a one-year history of vague digestive distress and a two-month history of gradually increasing painless jaundice with dark urine and acholic stools. He had lost twenty pounds in the preceding three months and over fifty pounds in the preceding two years. The remainder of the history was irrelevant, except for a story of dyspnea on exertion.

Examination revealed nothing outside normal limits except for jaundice and emaciation. The laboratory work showed hemoglobin 12 Gm. per 100 c.c. of blood. Serum bilirubin was 14.1 mg. per cent. The urine was normal except for bile pigments. Pulse was 60; blood pressure, 109/65; height, 74 inches; weight, 157 pounds clothed. Quantitative examination of the stool for urobilinogen showed passage of 0.7 mg. daily, indicative of complete biliary obstruction and, therefore, carcinomatous obstruction (Watson).

He was given a high vitamin, high protein diet including parenteral vitamin K preoperatively.

Operation.—On Jan. 2, 1942, with a weight of 139 pounds, the patient was transferred to the surgical service and taken to the operating room. The operation was started under cyclopropane, but the anesthetic was changed to ether and oxygen shortly because of the development of auricular fibrillation. Through a long transverse incision, one-third of the way from the umbilicus to the xyphoid, the abdomen was opened. A vertical extension was made upward in the right rectus muscle later in the procedure.

A small discrete tumor was found in the region of the head of the pancreas. It was placed rather high (cephalad) in the head of the pancreas. There was no evidence of spread of the tumor within the peritoneal cavity except for three small irregularities on the surface of the liver. Inasmuch as these irregularities could not be definitely considered to be carcinoma, and in any case did not seem to justify abandonment of all operative procedure, it was decided that radical one-stage resection of the head of the pancreas and duodenum should be performed. The lower end of the stomach was dissected free, and the pylorus was cut between clamps. The lateral avascular ligament of the duodenum was cut down as far as the mesocolon and the duodenum with the tumor attached to the internal margin was rotated forward. Dissection was carried down to the uncinate portion of the head of the pancreas, which was dissected free from the third portion of the duodenum. The

the lower half of the stomach and of the entire duodenum. To prevent subsequent cholangitis, internal biliary drainage with a *wide stoma* is accomplished by end-to-end cholecystojejunostomy, and regurgitation into the biliary system is rendered minimal or absent (as shown by roentgen study) by the use of a *long loop* between this anastomosis and the posterior Polya gastroenterostomy.

Pancreatic steatorrhea has followed exclusion of pancreatic secretion from the intestinal tract. Because of this occurrence in this case and in some cases reported elsewhere, consideration of reimplantation of the pancreatic duct into the bowel in such cases is being entertained both here and elsewhere.

ADDENDUM

After this paper had been prepared, an additional case of carcinoma of the head of the pancreas in a man of 67 has been subjected to resection of the lesion. Difficulties were encountered because of very low choledochocystic junction, which was involved in the lesion, and because of arterial anomalies consisting of absence of the celiac axis and origin of the hepatic artery from the superior mesenteric artery, the anomalous hepatic artery traversing the head of the pancreas. Considerable blood loss occurred following removal of the lesion, and large transfusions were necessary before satisfactory repair had been accomplished to the anomalous hepatic artery, the portal vein, the splenic vein, and an anomalous vessel springing from the left gastric to the left lobe of the liver. The procedure was completed with choledochenterostomy to the closed end of the jejunum brought through the mesocolon and Polya gastroenterostomy after hemigastrectomy. The patient, however, died shortly postoperatively. Autopsy showed a clean, dry operative field and massive pulmonary edema. Further arterial anomalies were also present.

REFERENCES

1. Bachrach, W. H., and Fogelson, S. J. Choledochojejunostomy. An Experimental Study After Resection of the Duodenum and Seven Eights of the Stomach, *STOMACH* 6: 582, 1939.
2. Brunswick, A., and Clark, D. E. Carcinoma of the Intrahepatic Portion of the Common Bile Duct, *STOMACH* 10: 573, 1941.
3. Coffey, Robert C. Pancreatoenterostomy and Pancreatectomy, *Ann. Surg.* 50: 1238, 1909.
4. Hunt, Verne C. Surgical Management of Carcinoma of the Ampulla of Vater and of the Perampullary Portion of the Duodenum, *Ann. Surg.* 114: 570, 1941.
5. Knusch, W. Ueber Gallenweg Darmerverbindungen, *Arch. f. klin. Chir.* 47: 574, 1912.
6. Martzloff, Karl H., and Burget, George E. The Closed Intestinal Loop. III. Aseptic End to End Intestinal Anastomosis and a Method for Making a Closed Loop Suitable for Physiologic Studies, *Arch. Surg.* 23: 26, 1931.
7. Morland, Randall B., and Freeman, Bromley S. Two Stage Resection of Carcinoma of the Ampulla of Vater, *STOMACH* 9: 712, 1941.
8. Trautmann, M., Robbins, H. J., and Stewart, C. C. An Experimental Study of the Operation of Cholecystenterostomy, *Surg., Gynec. & Obst.* 44: 612, 1927.
9. Trimble, I. R., Parsons, J. W., and Sherman, C. P. A One stage Operation for the Cure of Carcinoma of the Ampulla of Vater and of the Head of the Pancreas, *Surg., Gynec. & Obst.* 73: 711, 1941.
10. Wangensteen, Owen H. Cholangitis Following Cholecystenterostomy, *Ann. Surg.* 87: 54, 1928.
11. Wangensteen, Owen H. Aseptic Gastric Resection, *Surg., Gynec. & Obst.* 70: 58, 1910.

a few grains of sulfathiazole between rows of sutures, a retrocolic Polya gastro-jejunojejunostomy was performed much as described by Wangensteen. It had been planned to do a Coffey type of anastomosis between the tail of the pancreas and the jejunum below the gastrojejunostomy, but the patient's condition was not satisfactory, inasmuch as he had been having fibrillations for some time and the blood pressure had fallen below 100 mm. Hg. A cigarette drain was brought down to the cut end of the pancreas after all large vessels in the neighborhood and also the ligated end of the common duct had been covered with omentum. The end of the rubber drain was sutured anteriorly and posteriorly to the cut end of the pancreas in such a fashion that any leakage from it would have to escape through the drain, and a tunnel of omentum was made with catgut sutures to surround the drain to a stab wound placed about 6 cm. below the midportion of the incision, a precaution to prevent drainage from reaching the line of closure. Approximately one gram of sulfathiazole was placed in the region of the cut surface of the pancreas. The incision was closed with interrupted five-pound test silk, with implantation of a few more grains of sulfathiazole. The patient received 1,500 c.c. of blood and 400 c.c. of plasma during the seven-hour procedure, and left the operating room in fair condition.

Postoperative Course.—Postoperatively the patient went into acidosis, and the blood sugar rose to 230 mg. per cent, a result attributed to manipulation of the pancreas. The daily administered 20 per cent dextrose solution (1,000 c.c. daily) was, therefore, accompanied by 60 units of insulin per liter the first two days, following which the insulin requirement rapidly disappeared. Immediately postoperatively the patient was digitalized rapidly, but continued to have auricular fibrillation for several days. On the third day bile stained fluid drained through the cigarette drain, and this persisted for thirteen days, the daily volume diminishing gradually from an original 200 c.c., and the bile content also decreasing. A small stitch abscess occurred at fourteen days, but healing occurred quickly on drainage. The cigarette drain was removed at fourteen days. A trial on pancreatic juice obtained from a canine pancreatic fistula prior to dismissal resulted in nausea. He was therefore placed on pancreatin* and polyvitamin capsules on dismissal twenty-one days after operation.

Following dismissal the patient gained ten pounds in eight weeks, and improved in general health and strength. On March 28, he had begun to lose weight and was observed to have bulky, fatty, foamy, strong smelling stools. He also complained of nausea on ingestion of sweet foods. For these reasons he was readmitted for study. A gastrointestinal roentgen study showed rapid emptying of the gastric pouch with no regurgitation of the contrast medium into the proximal jejunal loop. There has been no evidence of cholangitis and no overt evidence of recurrence at the present writing, three and one-half months postoperatively. Preliminary studies indicate absorption of only 65 per cent of ingested fat; further studies are being performed. The patient has ceased losing weight at 129 pounds, following institution of a special diet.†

CONCLUSION

An operative procedure for carcinoma of the head of the pancreas has proved successful in one case. It encompasses excision, also, of

*Eli Lilly and Company.

†After this paper had been submitted for publication, this patient returned with recurrence in the line of incision. Roentgen therapy has been employed, but he is losing ground rapidly at this time (June 24).

PROBLEMS WITH DUODENAL STUMP IN GASTRIC RESECTIONS

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PARTIAL gastric resection has come to be employed frequently in the treatment of benign and malignant lesions of the stomach and duodenum. After it was shown that gastroenterostomy was followed by a considerable number of stomal and jejunal ulcers, many surgeons abandoned this procedure and turned to partial gastric resection as the operation of choice.

The operation of resection is a much more formidable procedure than gastroenterostomy and the technical difficulties are so many that a well-established routine must be developed before a surgeon can expect to escape many of the hazards of this operation.

Most of the articles which have been published on the subject of gastric resection have directed attention to the varied techniques used in establishing the anastomosis between the cut end of the stomach and jejunum. The importance of proper closure of the duodenal stump in the Polya-Reichel or Hofmeister-Finsterer type of Billroth II partial gastrectomy is undoubtedly appreciated by surgeons. Clute¹ has stated that no part of a gastric resection is more likely to be followed by fatal complications if improperly done than the closure of the duodenal stump. Yet critical evaluations of this problem and significant contributions toward improving and strengthening the closure have been sparse.

In this paper we propose to discuss certain methods and techniques which we have found helpful in the prevention of postoperative complications arising from the closed blind-ended duodenal stump.

Complications.—Following gastric resection, hemorrhage may occur which not uncommonly destroys the life of the patient. This may take place within the duodenal lumen from an unresected ulcer, or into the peritoneal cavity from injury to the gastroduodenal artery or its branches. Another complication may be the development of an abscess due to leakage from the closed duodenal stump. Still another possibility is that of frank disruption of the closed stump. In the case of abscess formation or disruption of the sutured duodenum, there not infrequently follows a duodenal fistula which permits the duodenal contents to pour out over the skin of the upper abdomen. The latter complication has a very high mortality rate.

12. Watson, C. J.: Studies of Urobilinogen. III. The *per diem* Excretion of Urobilinogen in the Common Forms of Jaundice and Disease of the Liver, Arch. Int. Med. 59: 206, 1937.
13. Whipple, A. O.: Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas, Am. J. Surg. 40: 260, 1938.
14. Whipple, A. O.: Present-Day Surgery of the Pancreas, New England J. Med. 266: 515, 1942.
15. Whipple, A. O., Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, Ann. Surg. 102: 763, 1935.
16. Orr, T. G.: Personal Communication to Owen H. Wangensteen.

The presence of the common duct in this region presents an additional hazard. In pursuing the attempt to close adequately the duodenal stump, several cases have occurred in which the common duct has been completely obstructed (Fig. 1, C). This is a most unfortunate accident, as it necessitates extensive surgery and reconstruction for its relief. The fact that a mild transient jaundice, due to angulation or temporary

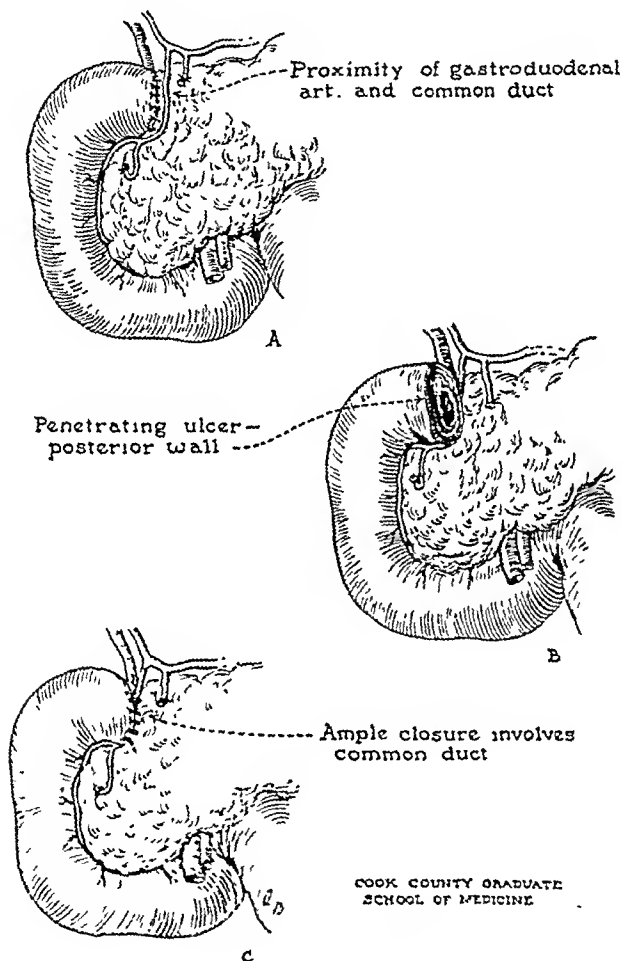


Fig. 1—Problems and accidents common in closure of the duodenal stump.

compression of the common duct, not infrequently appears following a gastric resection and rights itself after a few days, is undoubtedly responsible for unwarranted delay in these cases where the common duct is completely obstructed by its involvement in the duodenal closure. In the hope that each case of postoperative icterus may be of the temporary type, further surgery is not attempted until the condition has shown no tendency to improve spontaneously and the patient is deeply jaundiced.

These complications may be due to a combination of various factors in any one case, but in order to present the subject more clearly and to emphasize the importance of each factor, the problem will be discussed under two main headings: 1. The location of the ulcer; 2. The intraluminal pressure in the duodenal stump.

LOCATION OF THE ULCER

Portis and Jaffe,² in a recent study of peptic ulcer based on necropsy records, found that 62 per cent of 158 duodenal ulcers were located on the posterior wall of the duodenum, while 38 per cent were on the anterior wall. When the ulcer is on the anterior wall of the duodenum, close to the pyloric vein, closure of the stump presents comparatively few difficulties. Such ulcers are also the least likely to have had hemorrhages of great severity. When the ulcer is located on the posterior wall of the duodenum, however, there is much greater likelihood of its having been complicated by massive hemorrhage or by pyloric stenosis.

These complications, hemorrhage and stenosis, often make operation necessary. The extreme importance of adequate preparation for surgery, which, in the case of hemorrhage, should include multiple transfusions, cannot be stressed too much. However, the technical details of surgical management in such cases are of equal importance. If the operation is done for hemorrhage, one frequently finds that a large branch of the gastroduodenal artery has been eroded and lies in the depths of the penetrating ulcer, surrounded by pancreatic tissue. The ulcer is often near the duodenohepatic ligament and not infrequently this region is infiltrated and edematous. To isolate and ligate the gastroduodenal artery above the convexity of the duodenum has been suggested as a means of controlling hemorrhage from the eroded vessel in the ulcer depth. It is necessary, however, to ligate the artery below the duodenum where it branches into the pancreatic and epiploic divisions. The collaterals in this area are so numerous that it is a great problem to isolate and ligate accurately all of the major branches which might contribute to severe bleeding due to erosions involving the gastroduodenal artery as it passes behind the first portion of the duodenum. If the operation is done for pyloric stenosis, the obstruction of the gastric outlet may be found to be due to the edema and inflammatory infiltration resulting from the ulcer's penetration of the head of the pancreas (Fig. 1, *B*). In either of these cases, if one were to attempt to free up this duodenum from the pancreas and carry the dissection beyond the ulcer, considerable difficulty would be encountered in establishing a line of cleavage and in maintaining the continuity of the duodenal wall. The tissues are inclined to be thickened and friable and the bleeding following dissection is often profuse. The proximity of the main trunk of the gastroduodenal artery adds to one's difficulties (Fig. 1, *A*). Even if one were successful in freeing up the duodenum, there still would remain the problem of mobilizing enough wall for an inversion which would be adequate to prevent leakage or actual disruption.

In the last method, in every instance, the duodenum ruptured first at the site of the transverse stitches under pressures higher than those to which the human duodenal stump would ever be subjected (222 mm. of mercury), thus demonstrating the added protection which the transverse plication gives to the duodenal stump.

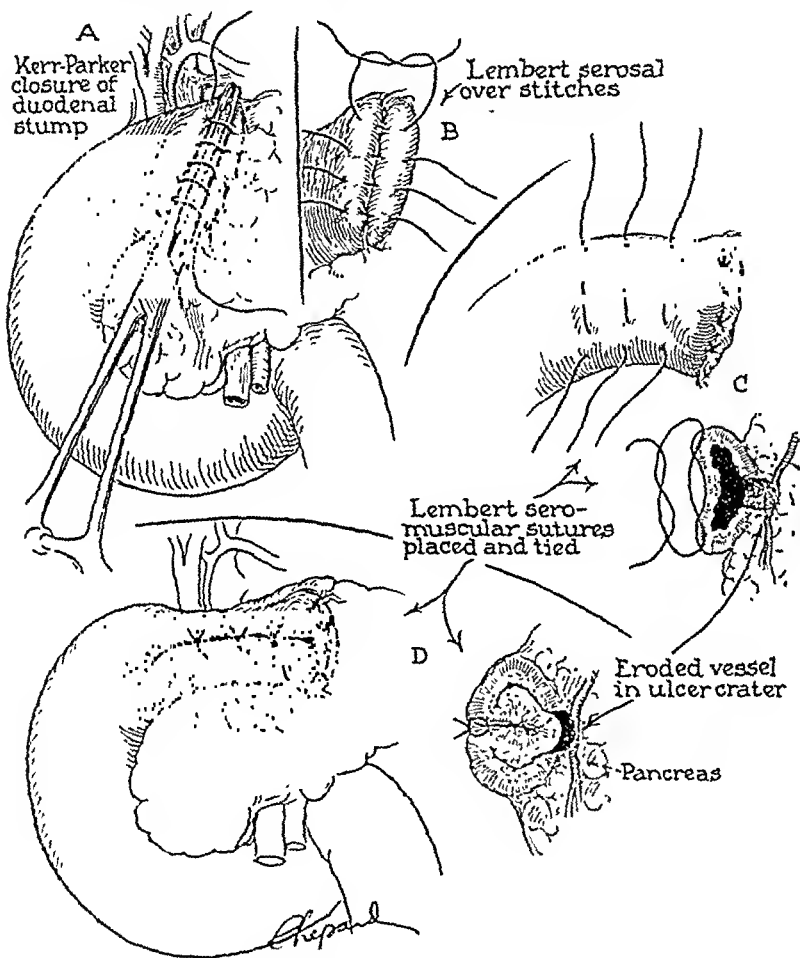


FIG. 2.—Steps in duodenal tamponade.

INTRALUMINAL PRESSURE IN THE DUODENAL STUMP

When gastric secretion has been diverted, there still remains the flow of the bile and pancreatic juices into the proximal duodenum. This is also augmented by the secretions of the mucosa itself. The total amount of these secretions may vary within wide limits, but generally can be said to be in the neighborhood of 1,000 to 1,500 c.c. in twenty-four hours. With such an amount of fluid pouring into this short portion of the intestinal tract, one can understand readily that any inter-

From this brief discussion it becomes obvious that the vulnerable posterior wall of the duodenum is one of the principal hazards in gastric resection.

The necessity for resecting the ulcer area in such cases does not seem to be great, as there is a marked tendency for these ulcers to heal as soon as gastric secretion is completely diverted. Ginzburg and Mage,⁴ in a recent study, found that 56 of 58 duodenal ulcers from which the gastric secretion had been diverted had healed.

In these cases of posterior wall ulcer we have found a great advantage in a method of closure which we have termed "closure of the duodenum with tamponade." In brief, it is developed along the following lines.

The duodenum is divided between clamps at or near the pyloric orifice. The proximal duodenum is freed up very cautiously and no attempt is made to resect the ulcer area on the posterior wall. After preliminary closure of the stump with a Kerr-Parker stitch or simple over-and-over suture (Fig. 2, *A* and *B*), the duodenum is then plicated longitudinally for a distance of one to one and one-half inches (Fig. 2, *C* and *D*). This practically always extends beyond the ulcer crater, which is on the posterior wall. The purpose of the plication is to crowd the anterior free wall down into the penetrating ulcer crater on the posterior wall, as shown in the diagrammatic cross-section of Fig. 2, *D*. In many ways this procedure follows the principles of the obliterative aneurysmorrhaphy of Matas. The enfolding not only tamponades the ulcer from which the hemorrhage, if any, has come, but it also protects the weak stump from leakage and disruption. This is explainable on the basis that the transverse plication and narrowing give an added reinforcement and take the pressure from the inverted duodenal stump.

Fogelson and his co-workers³ have undertaken to work out on dogs an accurate quantitative measurement of the various methods of duodenal stump closure. They felt that the best method for measuring the strength of the closure would be to determine how much air pressure was necessary to blow out the stump. This was done by sectioning the duodenum of a dog at its distal untraumatized end (after a Polya type of gastric resection had been done), inserting a glass tube, which was then tied in place, and connecting the tube to a bicycle pump through a specially constructed large size mercury manometer. The intraluminal pressure of the duodenum could thus be increased until rupture occurred, at which moment the pressure reading on the manometer was noted. The five different methods of closure employed were as follows:

1. Von Haberer open method without clamps or crushing.
2. Crushing clamp method of Kerr-Parker.
3. Simple ligature followed by purse string without clamps or crushing.
4. Same as method 3, using silk instead of catgut.
5. Duodenal tamponade in addition to Kerr-Parker clamp method.

are bound to be created where the jejunum is fixed to the greater curvature and the lesser curvature of the stomach. Certain errors in handling the anastomosis may accentuate this angulation, which may result in partial or complete obstruction of the jejunal lumen. This in turn may create a closed loop obstruction of the duodenum. This was well pointed out by Raffel⁶ recently when he said, "The cause of disruption of the duodenal suture line is believed by some surgeons to be obstruction (early) at or near the stoma of the anastomosis, and large quantities of duodenal contents are found in the peritoneal cavity when this complication occurs."

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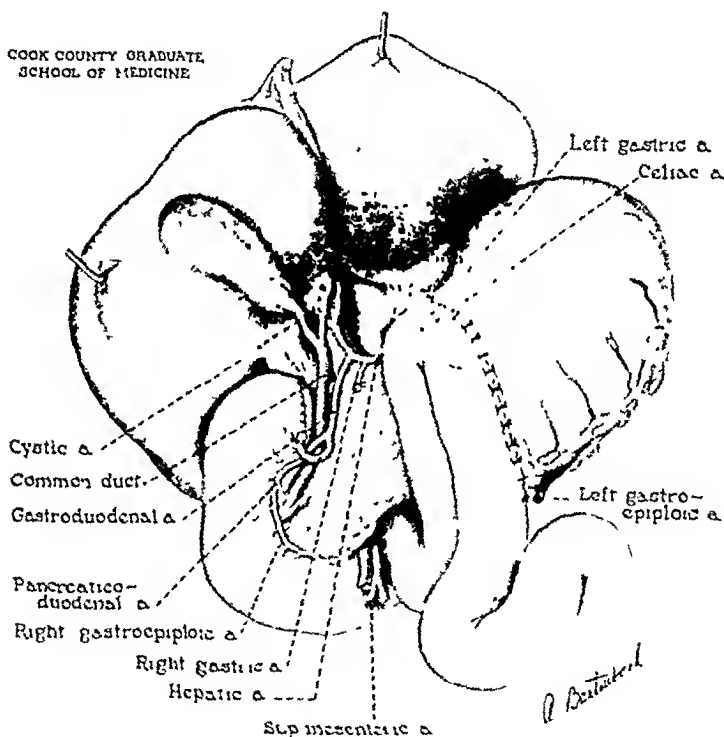


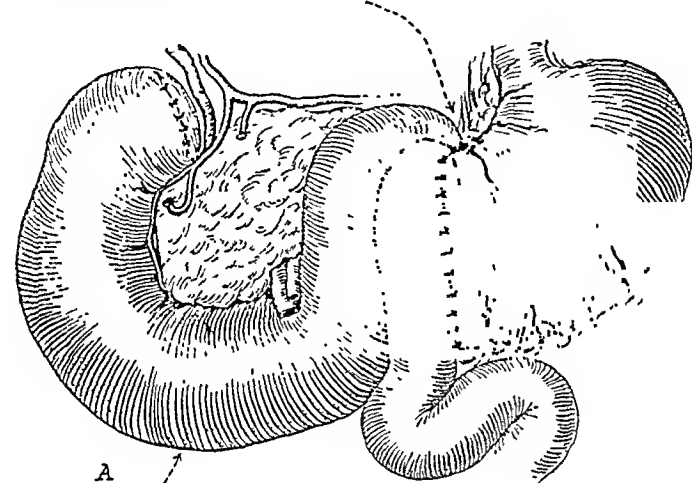
Fig 4—Properly managed anastomosis

Errors in handling the anastomosis may be rather arbitrarily divided into three groups. (1) In some instances, the obstruction may result from the manner in which the stomach and anastomosed jejunum are delivered through the transverse mesocolon, (2) obstruction may be due to an improper suturing of the transverse mesocolon to the stomach proximal to the gastrojejunal anastomosis line, (3) jejunal angulations may result from the improper suturing at the lesser and greater curvature angles of the anastomosis.

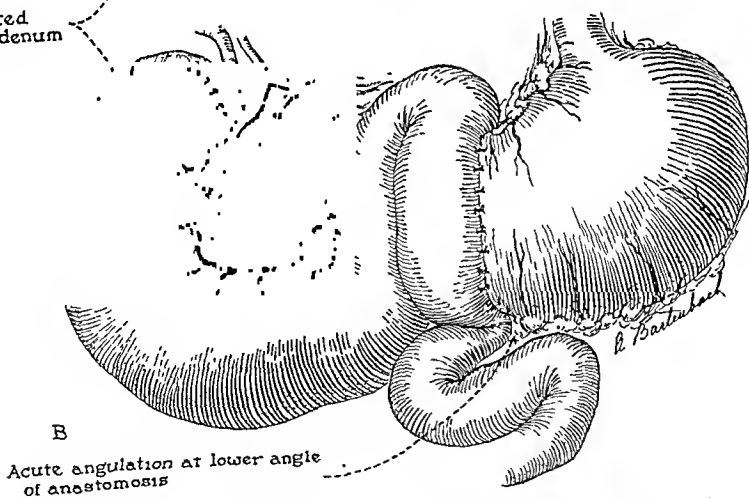
ference with the outflow of this secretion would produce within a short time a considerable accumulation and pressure within this segment. Wangensteen⁷ has reported that in an obstructed duodenum in a dog, the intraluminal pressure varies between 20 and 45 cm. of water pressure. In 1929, Dragstedt² called attention to the fact that the duodenum was more rapidly and severely susceptible to the effects of distention than any other portion of the intestine.

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Acute angulation at upper angle
of anastomosis



A
Dilated
duodenum



B
Acute angulation at lower angle
of anastomosis

Fig. 3.—Errors in anastomosis which lead to closed loop obstruction of the duodenum.

Let us, therefore, direct our attention toward this mechanical obstruction to the outflow of the duodenal contents.

When an anastomosis is made between the cut end of the stomach and the antimesenteric border of the jejunum, rather sharp angulations

it lies in the ulcer bed surrounded by pancreatic tissue. In these cases and in cases of pyloric stenosis due to edema and inflammatory infiltration resulting from the ulcer's penetration of the head of the pancreas, it is often extremely difficult to free up the duodenum from the pancreas and carry dissection beyond the ulcer. Even if one were successful in freeing up the duodenum, there would still remain the problem of mobilizing enough wall for an inversion which would be adequate to prevent leakage or actual disruption. There is also the dangerous possibility of involving the common duct in an adequate closure of the duodenum.

It is my feeling that too much emphasis has been placed on the necessity of resecting the ulcer itself, particularly in cases of penetrating posterior wall duodenal ulcers. Even the most chronic of these tend to heal when gastric secretion has been diverted.

A method of duodenal closure has been presented, which I have found particularly helpful, both in lessening the number of hemorrhages, and in protecting the weak stump against the back pressure which under ordinary circumstances might encourage it to blow out. Hemorrhage is prevented by crowding the anterior wall of the duodenum down to act as a plug to the ulcer bed on the posterior wall. Pressure on the duodenal stump is alleviated by the transverse plication and narrowing of the duodenal lumen just proximal to the stump.

The various technical errors which lead to marked increase of intraluminal pressure of the duodenum can be avoided by scrupulous attention to the mechanics of the gastrointestinal anastomosis.

REFERENCES

1. Clute, H. M.: Duodenal Stump Closure in Gastric Resections With a Modified Furniss Clamp, *New England J. Med.* 214: 724, 1936.
2. Dragstedt, C. A., Lang, V. P., and Millet, R. F.: The Relative Effects of Distention on Different Portions of the Intestine, *Arch. Surg.* 18: 2257, 1929.
3. Fogelson, S. J., Slive, A., and Shoch, D.: Personal communication.
4. Ginzburg, L., and Mage, S.: Failures Following Gastro-Enterostomy for Gastroduodenal Ulcer, *Surg., Gynec. & Obst.* 67: 788, 1938.
5. Portis, S. A., and Jaffe, R. H.: A Study of Peptic Ulcer Based on Necropsy Records, *J. A. M. A.* 110: 6, 1938.
6. Raffel, W.: A New Method for Physiologic Decompression After Gastric Operations: Preliminary Report, *Arch. Surg.* 42: 1083, 1941.
7. Wangensteen, O. H.: Aseptic Resections in the Gastro-Intestinal Tract With Special Reference to Resection of the Stomach and Colon, *Surg., Gynec. & Obst.* 72: 257, 1941.

Fig. 3, *A* illustrates an angulation produced at the lesser curvature. The use of the technique suggested by Finsterer for protecting this site, that is, the suturing of the proximal loop of the jejunum to the lesser curvature of the stomach for a distance of 1 to 2 cm. above the corner of the anastomosis, may account for some of the obstruction in this region. If his method is correctly used, no angulation will occur, but if the corner is sutured too high along the lesser curvature, angulation is very likely to result. This will cause obstruction to the outlet of duodenal contents, and greatly increase the intraduodenal pressure.

In illustration *B* of Fig. 3, an angulation is shown at the greater curvature. This may be produced by carrying the jejunum around the greater curvature angle in order to make it seem more secure, or it not infrequently results from torsion of the anastomosed jejunum during the procedure of serosal suturing. When the angulation occurs at the greater curvature, there would seem to be even more risk of frank disruption of the closed duodenal stump. This is due to the fact that the secretions and regurgitated contents of the stomach are added to the secretions which arise in the duodenum and are brought there through the ampulla. The forceful contractions of the remaining fundic portion of the stomach may increase greatly the pressure within the proximal duodenum.

If the angles of the anastomosis are kept in proper alignment, these unfortunate conditions should not develop, that is, by placing the beginning sutures of the anastomosis exactly through the antimesenteric border of the jejunum and the greater curvature, and by finishing the anastomosis exactly at the antimesenteric border of the jejunum and the lesser curvature. Fig. 4 shows a completed anastomosis wherein the angles of the anastomosis are properly managed.

Raffel has suggested a method for decompressing not only the stomach, but also the duodenal loop, which in addition makes it possible to feed back into the normal distal jejunal loop the secretions collected from the stomach and duodenum, plus such exogenous material as might be required. The rationale and wisdom of such a procedure seem obvious, and it might well offer a further protection against leakage and disruption of the closed duodenal stump.

SUMMARY

While the importance of adequate duodenal stump closure in gastric resection is recognized by most surgeons, critical evaluations and contributions to strengthening and improving the closure have been sparse.

When resection is done for an ulcer on the vulnerable posterior wall of the duodenum, the difficulties of closure of the duodenal stump are greatly increased. In the case of hemorrhaging peptic ulcer, failure can be attributed frequently to the technical steps which do not efficiently prevent recurrence of hemorrhage. In many instances the bleeding is from an open eroded vessel which cannot be successfully approached, as

Numerous examples of benign gastric tumors have been described accurately in the literature since one of the earliest cases was reported by Gibson before the New York Surgical Society in 1907. With an increased appreciation of the clinical findings in these cases and with the refinements of modern roentgenologic technique, there should be little difficulty in making the diagnosis of benign gastric polyp. My own experience with these cases, however, has convinced me that examples of these benign tumors are constantly being overlooked. The importance of recognizing them early lies in the fact that such tumors are frequently the cause of serious complications. To quote Conway: "The fact that a new growth of the stomach may be benign assumes a practical aspect in view of the importance of conserving such an organ as the stomach." Early diagnosis, followed by immediate operation, obviously will avoid these complications.

Malignant degeneration is the gravest complication which may occur in these tumors. In fifty-eight cases of benign gastric tumors (which included all types of tumors, such as the fibromas, lipomas, and adenomas) reported by Balfour and Henderson in 1927, malignant degeneration was found in only two or 3.5 per cent. The percentage of malignant degeneration is not found to be so low in other series of cases, nor in those cases in which the condition has existed unrecognized for a comparatively long period of time. As a matter of fact, adenomatous polyps and leiomyoma are especially prone to undergo malignant degeneration. McRoberts, reporting from the Mayo Clinic in 1933, presented five cases of adenoma of the stomach which he personally had observed during the preceding year and one-half. In four cases, or 80 per cent, meticulous study of serial sections revealed unquestionable evidence of malignant change. In a series of adenomatous polypi carefully studied by Eliason and Wright, carcinomatous change was found in eight of twenty-three cases, an incidence of 35 per cent. In 1934, Benedict and Allen reported seventeen cases of gastric polypi from the records of the Massachusetts General Hospital, and in this group seven, or 41.2 per cent, showed evidence of malignant degeneration. In a recent publication by Lahey and Colcock, five out of seven of the patients, or 71 per cent, operated upon in the Lahey Clinic for leiomyomatous tumors, showed sarcomatous degeneration. In the New York Hospital series of nine cases, three of them, or 33½ per cent, had become malignant.

The next most important complication of these gastric tumors is hemorrhage. Anemia and the presence of occult blood is greater in association with this condition than with ulcer of the stomach. Severe bleeding, with hematemesis and melena, while it may occur, is not characteristic of benign gastric polypi, but moderate bleeding, with gross or occult blood in the stool, is quite common. Anemia is one of the most frequent and characteristic signs of benign tumor of the stomach. The

BENIGN TUMORS OF THE STOMACH*

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THE purpose of this paper is to review nine cases of benign tumors of the stomach gathered from the records of the New York Hospital since its opening in September, 1932, through December, 1940. Three of the nine cases had already become malignant at the time of operation, leaving a total of six tumors in the above period which could be classified strictly as benign. Abstracts of the histories and findings in these cases will be noted at the end of the paper.

In the group of nine cases described, the average age was 44 years; the youngest patient was 24 years of age, and the oldest, 58. The incidence of sex is unusual, in that of the entire group of nine cases only one patient was a male.

Benign tumors of the stomach are not common. When one considers the number of roentgenologic examinations of the stomach that are made each year at the New York Hospital, the incidence of benign tumor is very small, for in the x-ray department an average of about twenty examinations of the stomach are made each day. The number of working days in a calendar year at the hospital is about 270. This means that, in round numbers, 5,400 roentgenologic examinations are made of the stomach yearly, and for the period included in this report (eight years) the number of examinations approximate 43,200. During this time only six benign tumors of the stomach were found. The ratio, then, of the number of benign tumors to the number of roentgenologic examinations of the stomach at New York Hospital is about 1 to 7,200.

In the past the ratio of malignant to benign tumors of the stomach was given as about 200 to 1. At the New York Hospital within the period noted above, there were 289 patients with carcinoma of the stomach admitted to the pavilions. The life histories of these patients are being studied carefully by Dr. William A. Cooper. One hundred and five more cases of carcinoma of the stomach were seen on the private and semi-private services. Three hundred and ninety-four cases, then, of carcinoma of the stomach were seen during this period of time in which we collected the data on six benign tumors. The ratio of malignant to benign tumors, therefore, was much less than 200 to 1 and was in fact about 66 to 1.

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following roentgenologic findings are characteristic of benign :

they produce a filling defect that is circumscribed and punched appearance.

The filling defect is usually on the gastric walls, leaving the mucosa regular and pliant.

In inflammatory and malignant lesions, the rugae are obliterated in the immediate area of the tumor, but the rugae surrounding a benign tumor are nearly normal in their arrangement and distribution.

They cause little or no disturbance in peristalsis and retention is uncommon, except when the lesion is at or near the pylorus.

They do not reveal a niche, nor is there any incisura or other evidence of spasm.

They are rarely sufficiently large to be palpated.

If a polypoid tumor prolapses into the duodenum, it will produce a translucent shadow in the bulbous shadow which is typical. This occurred in one of our cases in which the diagnosis was made before operation. It is true, therefore, that the diagnosis of benign tumor of the stomach is being made more often and more confidently in the present time than has been in the past.

PATHOLOGY

Benign tumors may arise from any of the several coats of the stomach according to the tissue of origin, may be divided into epithelial and mesenchymal. Included in the epithelial group are the adenomas, papillomas, adenomyomas and fibroadenomyomas, fibromas, lipomas and the rare angiomas and osteomas. The leiomyomas, the most common of the benign tumors, constitute about 35 per cent of all benign tumors of the stomach. In a review of the literature by Minnes and Pickert, who collected 931 cases, 341, or 36.6 per cent, were leiomyomas. In the group of cases reported by Eliason and Wright, 60 per cent were leiomyomas. However, in the nine cases of our series which were operated upon and subjected to histologic examination, there was one leiomyoma and one leiomyosarcoma. Seven tumors were of the type commonly called polyps, that is, epithelial adenomas.

TREATMENT

In the majority of cases of benign tumors of the stomach, local excision, rather than resection, is indicated. The situation of the tumor, of course, determines the best approach. The procedure most frequently used in our series was transgastric excision, performed through an incision in the anterior wall of the stomach, and division of the mesogastric membrane pedicle. In operating on the large tumors, and in those cases in which the frozen section indicated malignant change, partial gastrectomy was the procedure of choice.

anemia is usually of the secondary or microcytic type, but in long-standing cases it may progress until it is suggestive of the primary type. Patients with obscure anemias or pernicious anemias should be subjected to roentgenologic examination of the gastrointestinal tract. In this connection it is interesting to note that in seventeen cases reported by Benedict and Allen from the Massachusetts General Hospital, primary anemia was the first diagnosis in five, or an incidence of 30 per cent. In our own series of nine cases, a primary diagnosis of pernicious anemia was made in two cases, but a moderate to severe secondary anemia was present in all the others.

SYMPTOMS AND SIGNS

Benign tumors of the stomach, as a rule, do not cause marked symptoms unless they are complicated by bleeding or intermittent obstruction of the pylorus, or unless because of their size and extent they interfere with gastric motility and secretion. Given a patient with anemia and achylia gastrica, who on x-ray examination reveals the characteristic punched-out smooth defect in the stomach or first portion of the duodenum, the diagnosis of benign tumor of the stomach is certain. Absence of free hydrochloric acid in the gastric contents was a constant finding in our cases. Pyloric obstruction, usually intermittent, occurs in a small percentage of the cases. These are the ball-valve type of tumors which are attached to the posterior wall of the stomach and develop a long mucous membrane pedicle, at first obstructing the pylorus in the manner of a ball-valve and then, finally, prolapsing into the duodenum, where they remain. Our series includes one of these interesting tumors, which was seen by x-ray and diagnosed as a benign tumor of the stomach which had herniated through the pylorus into the duodenum. On roentgenologic examination in this case, the tumor appeared to be entirely within the duodenum and to have its origin there, but exploration disclosed that its pedicle was on the gastric side of the pylorus. There are no characteristic digestive symptoms which produce a syndrome on which the diagnosis of benign tumor could be made.

ROENTGENOLOGIC FINDINGS

With expert radiologic examination of the stomach, a greater number of accurate diagnoses have been made. Benign tumors present certain roentgenologic signs which differentiate them from malignant or inflammatory lesions. However, the differentiation cannot always be made with certainty by means of x-ray. One of the most interesting cases reported in this group was a case of tumor of the stomach which had been diagnosed by x-ray as an inoperable carcinoma. When it was decided to perform a palliative operation on this patient because of persistent vomiting, it was found that she had a benign tumor of the stomach which could be locally resected.

The following roentgenologic findings are characteristic of benign tumors:

1. They produce a filling defect that is circumscribed and punched out in appearance.
2. The filling defect is usually on the gastric walls, leaving the curvature regular and pliant.
3. In inflammatory and malignant lesions, the rugae are obliterated in the immediate area of the tumor, but the rugae surrounding a benign tumor are nearly normal in their arrangement and distribution.
4. They cause little or no disturbance in peristalsis and retention is uncommon, except when the lesion is at or near the pylorus.
5. They do not reveal a niche, nor is there any incisura or other evidence of spasm.
6. They are rarely sufficiently large to be palpated.

If a polypoid tumor prolapses into the duodenum, it will produce a central translucence in the bulbar shadow which is typical. This occurred in one of our cases in which the diagnosis was made before operation. It is true, therefore, that the diagnosis of benign tumor of the stomach is being made more often and more confidently in the present than it has been in the past.

PATHOLOGY

Benign tumors may arise from any of the several coats of the stomach and, according to the tissue of origin, may be divided into epithelial and mesenchymal. Included in the epithelial group are the adenomas, adenopapillomas, adenomyomas and fibroadenomyomas, fibromas, lipomas, and the rare angiomas and osteomas. The leiomyomas, the most common of the benign tumors, constitute about 35 per cent of all benign tumors of the stomach. In a review of the literature by Minnes and Geschickter, who collected 931 cases, 341, or 36.6 per cent, were leiomyomas. In the group of cases reported by Eliason and Wright, 60 per cent were leiomyomas. However, in the nine cases of our series which were operated upon and subjected to histologic examination, there was one leiomyoma and one leiomyosarcoma. Seven tumors were of the type commonly called polyps, that is, epithelial adenomas.

TREATMENT

In the majority of cases of benign tumors of the stomach, local excision, rather than resection, is indicated. The situation of the tumor, of course, determines the best approach. The procedure most frequently used in our series was transgastric excision, performed through an incision in the anterior wall of the stomach, and division of the mucous membrane pedicle. In operating on the large tumors, and in those cases in which the frozen section indicated malignant change, partial gastrectomy was the procedure of choice.

CASE REPORTS

All the surgical pathologic reports in the following cases were made under the supervision of Dr. N. Chandler Foot.

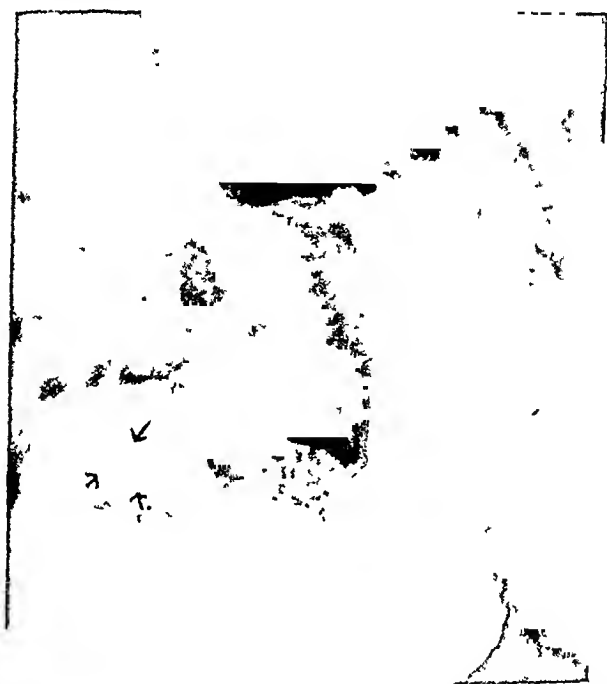


Fig. 1 (Case 1).—Typical punched-out and circumscribed filling defect of benign polyp in duodenal cap.



Fig. 2 (Case 1).—Spot film of same tumor shown in Fig. 1.

Case 1 is typical of a benign tumor which had prolapsed through the pylorus and had come to rest in the first portion of the duodenum. I personally observed it and did the operation, diagnosing it as a benign gastric polyp before operation.

CASE 1.—S. W. (New York Hospital No. 173873), female, aged 24 years, was admitted July 1, 1937, with a complaint of indigestion and weakness for the past three years. There was no history of any previous serious illness or operation. In 1935 she had been admitted to another hospital where she was treated for secondary anemia. For the past three years she had been suffering from epigastric distress and a feeling of fullness which came on in paroxysms. There had been no vomiting. In May, 1937, a gastrointestinal series revealed a central filling defect in the duodenal cap, which was not at that time interpreted correctly. A gastric analysis

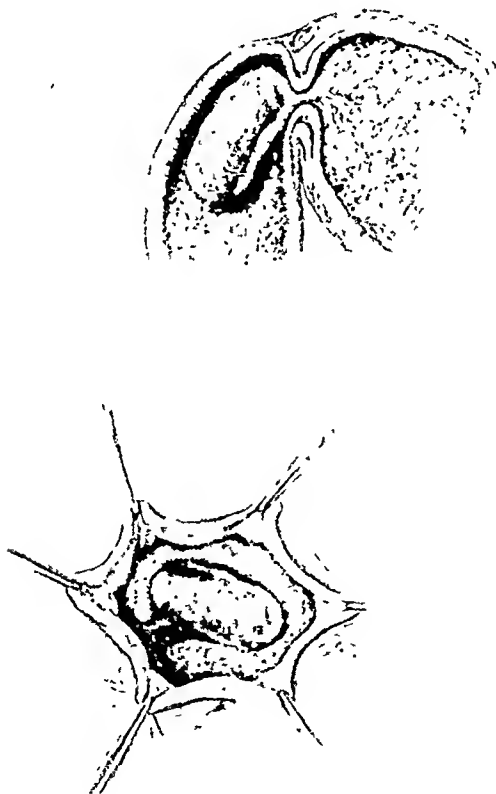


Fig. 3 (Case 1).—Drawing of polyp at operation. At top, note prolapse through pylorus into duodenum with mucous membrane pedicle attached to posterior wall of stomach. At bottom, note small incision through anterior wall of stomach showing polyp and pedicle just before excision.

revealed no free hydrochloric acid at this time. The physical examination was essentially negative. The abdomen was soft and no tumors were palpable. The hemoglobin was 75 per cent and two stool examinations were positive for occult blood. Fluoroscopy and roentgenograms of the gastrointestinal tract revealed a normal

stomach. The duodenal cap showed a displacement of barium measuring $2\frac{1}{2}$ cm. in its longest dimension (Figs. 1 and 2, Case 1). On one of the films there was a suggestive pedicle extending through the pylorus. The impression was that this was a gastric polyp which had prolapsed through the pylorus into the duodenum. At operation a small round, doughy tumor was palpated in the first portion of the duodenum. During palpation the tumor slipped back through the pylorus into the stomach. A short, longitudinal incision was made then on the anterior wall of the

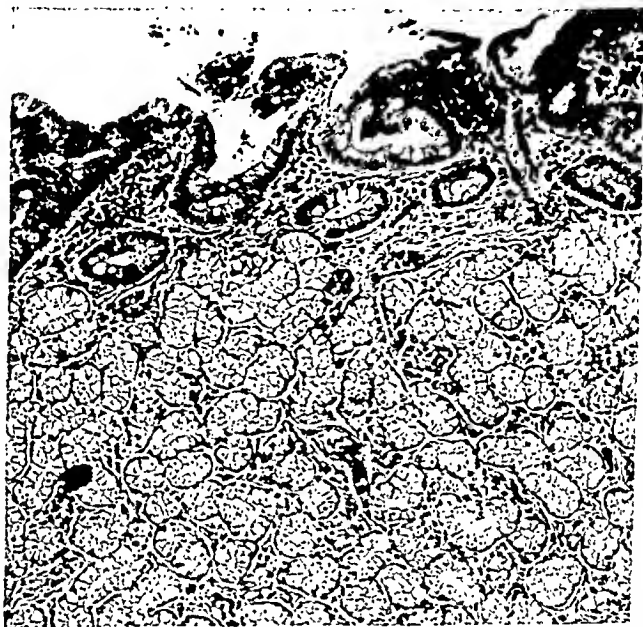


Fig. 4 (Case 1).—Section of polyp showing hypertrophied pyloric glands with a high degree of vascularization and numerous small areas of erosion of the covering epithelium.



Fig. 5 (Case 1).—X-ray six months after operation; normal stomach and duodenum.

stomach, just above the pylorus and midway between the two curvatures. On opening the stomach through this incision, a smooth round polyp with a mucous membrane pedicle was found attached to the posterior wall (Fig. 3, Case 1). This was excised with its pedicle, locally, and the stomach then closed transversely with mattress sutures of fine black silk. The abdomen was closed in layers with interrupted sutures of the same material. Convalescence was uneventful. The patient was discharged on the twelfth day after operation.

Pathologic Report.—The specimen is a polypoid tumor mass 22 by 13 by 7 mm. in size. It is soft and covered with reddened mucosa, which is in the main very smooth. On section it is found to be made up of glandular complexes which are putty colored and often umbilicated with a small red dot at the middle.

Microscopic Examination.—Most of the section is composed of hypertrophic glands which resemble Brunner's glands. Strands of fibrous tissue run between these glands, separating them into nodule-like areas. The covering epithelium shows a high degree of vascularization and numerous small areas of erosion, which probably account for the bleeding in this case (Fig. 4, Case 1).

Diagnosis: Benign polyp of the gastric mucosa.

X-ray examination of the gastrointestinal tract six months after operation showed the stomach to be normal throughout. The polyp is no longer seen either in the antrum or in the duodenal cap and the bulb fills well (Fig. 5, Case 1).

The patient reported three years after operation in good condition and with no symptoms referable to the stomach. The blood picture was normal.

In this second group are three cases of tumor of the stomach which had become malignant at the time of operation.

CASE 2.—P. O. (New York Hospital No. 127343), a woman, aged 43 years, was admitted March 30, 1936. Nine years before admission she began to have some epigastric discomfort with frequent eructations. Three years ago, because of the persistence of these gastric symptoms, her stomach was x-rayed and she was told that she had a tumor of the stomach. Six months before admission her symptoms became worse and were accompanied by daily aching pains in the upper abdomen and back. X-rays again revealed a tumor of the stomach. She had lost about fourteen pounds in weight. On admission, the physical examination was essentially negative, except that palpation of the abdomen suggested a mass in the mid-epigastrium. Laboratory examinations revealed 60 per cent hemoglobin with 3,500,000 red blood cell count. There was no free hydrochloric acid in the gastric contents after histamine, and the stool was positive for occult blood. Fluoroscopy and films of the gastrointestinal tract showed a lobulated lesion on the posterior wall of the pars media. The rest of the stomach and duodenum appeared to be normal (Fig. 6, Case 2). At operation a soft, polypoid, apparently benign tumor, was found, which arose from the anterior wall of the stomach and the pars media. The stomach was opened and the tumor locally excised. Frozen section, however, revealed a carcinomatous polyp. Accordingly, a gastric resection of the Polya type was performed.

Pathology.—The specimen consisted of a piece of tissue measuring $4\frac{1}{2}$ by 3 by $1\frac{1}{2}$ cm. in size, at one end made up of a pale mushroomlike mass $2\frac{1}{2}$ cm. in diameter and raised 1 cm. above the surrounding mucosa. The rest of the tissue was composed of reddened polypoid gastric mucosa. The consistence of the pale mass was very firm without being stony hard. Sections revealed the presence of a tumor of metaplastic glandular tissue. The glandular epithelium was extremely anaplastic in appearance and there were many mitotic figures present. There was deep infiltration of the tumor cells (Fig. 7, Case 2).

On follow-up three years after operation, the patient ate everything without distress and was working. Her color was good and the wound well healed. No

stomach. The duodenal cap showed a displacement of barium measuring $2\frac{1}{2}$ cm in its longest dimension (Figs. 1 and 2, Case 1). On one of the films there was a suggestive pedicle extending through the pylorus. The impression was that this was a gastric polyp which had prolapsed through the pylorus into the duodenum. At operation a small round, doughy tumor was palpated in the first portion of the duodenum. During palpation the tumor slipped back through the pylorus into the stomach. A short, longitudinal incision was made then on the anterior wall of the

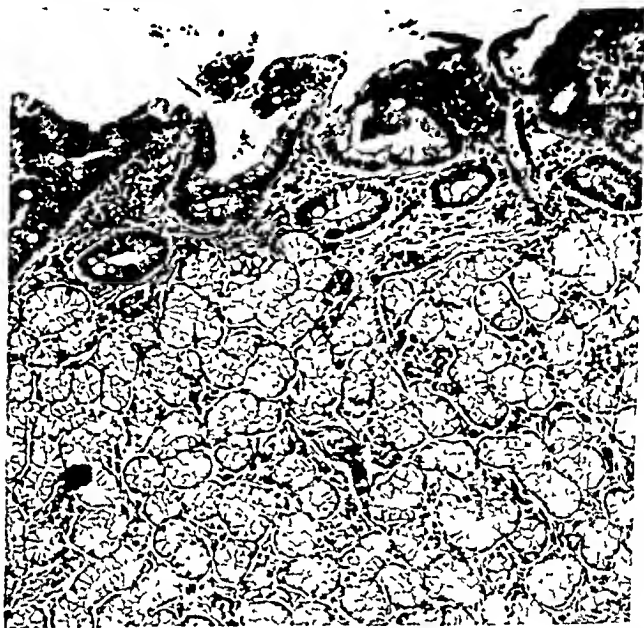


Fig. 4 (Case 1).—Section of polyp showing hypertrophied pyloric glands with a high degree of vascularization and numerous small areas of erosion of the covering epithelium



Fig. 5 (Case 1).—X-ray six months after operation, normal stomach and duodenum.

were excised and sent for biopsy. Frozen section was reported as carcinoma. It was decided that a resection of the pylorus or a gastroenterostomy was not justifiable. The diagnosis then was malignant polyp of the prepyloric region with multiple hepatic and peritoneal metastases.



FIG. 7 (Case 2).—Photomicrograph of malignant gastric polyp showing deep infiltration of anaplastic glandular epithelium.



FIG. 8 (Case 3).—Roentgenogram of the stomach showing the characteristic defect of a polypoid tumor at the pylorus.

masses were palpated in the abdomen, and the liver was not enlarged. Film and fluoroscopic examination of the gastrointestinal tract showed the stump of the stomach to be small in appearance, which was consistent with the previous operation. It emptied well and the remaining part of the stomach appeared to be normal throughout.



Fig. 6 (Case 2).—X-ray film of stomach showing lobulated lesion in the pars media.

CASE 3.—F. E. (New York Hospital No. 71840), a 52-year-old woman, was admitted Aug. 3, 1934, and discharged Sept. 12, 1934. This patient came in with a complaint of epigastric pain and distress. She also had an eleven-year-old story of diarrhea and generalized abdominal cramps due to mucous colitis. For two years previous to her admission, she had been very weak and had lost twenty pounds in weight. Her appetite was poor and there had been frequent spells of vomiting. On physical examination, she appeared to be fairly well nourished. No masses were palpated in the abdomen. Urine was negative, and hemoglobin 85 per cent with a red blood cell count of 3,980,000. In the gastric contents there was no free hydrochloric acid, even after stimulation with histamine. Fluoroscopy and films of the gastrointestinal tract showed an oblique stomach, medium in size and position. The duodenal cap had an unusual appearance. The barium seemed to be displaced by a foreign body. Findings were strongly suggestive of a polyp in the pyloric end of the stomach, probably malignant in character (Fig. 8, Case 3). When the peritoneal cavity was opened at operation, Aug. 17, 1934, about one liter of thin green fluid escaped. Edematous, boggy, indurated areas were found in the greater omentum. There were a number of small white deposits in the liver, 1 to 2 mm. in diameter. The stomach was explored and a mass found in the region of the pylorus. This could be moved from side to side within the lumen. It apparently rose from the posterior wall, or surface, of the prepyloric region and measured about 6 cm. by 2 cm. in size. Two small pin-point white deposits in the mesentery of the ileum

sleeve resection was done, leaving a margin of 4 cm. on either side of the excised tumor. No regional lymph nodes were seen or felt and there was no evidence of spread to the liver, omentum, or peritoneum.

Pathology.—The specimen consisted of a globular tumor from the stomach, measuring $4\frac{1}{2}$ cm. in diameter. It was covered on both sides by a thin layer of gastric mucosa which showed numerous pits or craters surrounded by elevated, nipplelike thickenings of the mucosa. The bulk of the tumor, however, seemed to lie below this



Fig. 10 (Case 4).—Photomicrograph of leiomyosarcoma of stomach showing spindle character of cells and many giant tumor cells.

and to be composed of a light-brown semigelatinous mass of tissue which was chiefly surrounded by the muscular layer of the stomach, although just within this a membranous capsule was apparently quite definitely seen. The tumor had a definitely sarcomatous appearance, and was very soft in consistency, except where it was attached to the gastric musculature, where it was quite firm.

Sections through the gastric tumor, described above in the gross, showed it to be an extremely cellular one. The cells varied markedly in size and shape, many of them being small spindle cells or oval in shape, and others round and epithelioid. Large numbers of giant tumor cells were present. These were undergoing all sorts of mitotic changes. All these cells were growing in a very loose stroma. After staining frozen sections with sudan III, fat cells could not be demonstrated, eliminating the possibility of this tumor being a liposarcoma and marking it as a fairly definite leiomyosarcoma of the stomach (Fig. 10, Case 4).

On July 25, 1939, one year after operation, roentgenologic examination of the stomach revealed the postoperative picture of a sleeve resection with no evidence of recurrence (Fig. 11, Case 4). At follow-up two years after operation, the patient was well and working.

Pathology.—The specimen consisted largely of fat, and sections showed in one area a number of tumor cells with indefinite cell outline, granular cytoplasm and oval dark-staining nuclei. These cells were poorly differentiated; many were vacuolated and a few mitotic figures were present. They tended at times to grow into acini, although many formed islands. There was definite invasion of both stroma and tumor cells to the omentum.

Follow-up revealed that this patient died at home, Oct. 25, 1935. No autopsy was performed.



Fig. 9 (Case 4).—Roentgenogram of the stomach showing area of increased radiability representing a probable benign tumor.

CASE 4.—A. L. (New York Hospital No. 205103), 29-year-old female, was admitted June 7, 1938, and discharged July 3, 1938. In April, 1937, this patient was admitted to the Rockefeller Hospital with marked hypertension. Examination disclosed a hydronephrotic kidney on the left. In April, 1938, a nephrectomy was performed at the Presbyterian Hospital and the blood pressure fell to 140, systolic. A checkup at the Rockefeller Hospital revealed a low hemoglobin, and a gastrointestinal series showed the presence of a gastric polyp. The patient also recalled having had tarry stools for two weeks prior to admission. There was no epigastric pain or distress. After admission to the New York Hospital with the above history, laboratory examinations revealed hemoglobin, 64 per cent, and red blood count 3,100,000. The stool was positive for occult blood. On June 9, 1938, films and fluoroscopy of the gastrointestinal tract showed a vertical stomach, medium in size and position, orthotonic, with normal peristalsis. There was a circular area of increased radiability in the body of the stomach representing a probable benign tumor (Fig. 9, Case 4). Operation through a left upper rectus incision disclosed a tumor in the stomach attached to the anterior wall, about 4 cm. in diameter. This tumor was excised with a small margin of normal stomach on all sides. Frozen section, however, showed the tumor to be a sarcoma. Since the tumor was in the mid-portion of the stomach a

Pathologic Report.—The specimen is a gastric polyp measuring about $3\frac{1}{2}$ cm. by 2 cm. Sections reveal a polyp with a stalk composed of loose connective tissue. The normal gastric mucosa changes its appearance fairly abruptly at the base of the polyp. The goblet cells are few in number and the nuclei are hyperchromatic. No mitotic



Fig. 12 (Case 5).—Reveals filling defect on posterior wall of stomach near the cardia.



Fig. 13 (Case 5).—Spot film showing filling defect characteristic of benign tumor.



Fig. 14 (Case 5).—Photomicrograph of section of benign polyp of stomach in a patient with pernicious anemia.

figures are seen and all the epithelial cells are arranged in very orderly fashion on the basal membrane without the least tendency to invasion of the underlying tissue. One has the impression, nevertheless, that these cells would become malignant on

A primary diagnosis of pernicious anemia was made in the following two cases:

CASE 5.—A. L. (New York Hospital No. 103630), a woman aged 58 years, was admitted Aug. 8, 1935, with a complaint of weakness. The patient's mother died of pernicious anemia and now one brother is said to be suffering from the same dis-



Fig. 11 (Case 4).—Roentgenogram of sleeve resection of stomach one year after operation. There is no evidence of recurrence.

order. Three years prior to admission to the hospital the patient had suffered from weakness and fatigue. She had had intermittent attacks of glossitis, numbness, and tingling of the toes. Just before admission there had been epigastric distress with a sense of fullness after eating. Liver therapy in the past had given some relief. Examination revealed a subicteric tint to the skin and conjunctiva. The tongue was not particularly smooth. The abdomen was soft and no masses were palpated. There was some loss of vibratory sense over the toes of both extremities. Laboratory examinations revealed no free hydrochloric acid in the gastric contents. There were 4,000,000 red blood cells, with 2+ stippling, macrocytosis; hemoglobin, 95 per cent. Films of the gastrointestinal tract showed a filling defect on the posterior wall near the cardia, about 3 cm. in size. This appeared to project into the gastric lumen, with the base appearing somewhat smaller, and the mass itself giving a pedunculated effect. The impression was that this patient had polyps or a hemangioma of the stomach (Figs. 12 and 13, Case 5).

On August 10, 1935, at operation through a left upper rectus incision, palpation of the stomach revealed the presence of a small tumor arising from the lesser curvature about midway between the cardia and pylorus, with a fairly narrow pedicle, the base of which did not seem to be invading the rest of the wall of the stomach. A wedge-shaped incision was used to excise the tumor and the defect was closed with chromic catgut. This catgut suture line was inverted with mattress sutures of fine black silk in the serosa.

In Case 7 there was pyloric obstruction and the x-ray diagnosis was carcinoma of the stomach.

CASE 7.—A. O. (New York Hospital No. 177671), a woman 54 years of age, was admitted Aug. 24, 1937, with a three months' history of epigastric pain associated with vomiting attacks lasting three or four days. Three days before admission she had an attack of abdominal pain with nausea and vomiting, so that even liquid foods were vomited immediately after ingestion. There was a loss of twenty pounds in



Fig. 16 (Case 7).—Roentgenogram of stomach showing the defect in the pyloric region diagnosed as carcinoma, which at operation proved to be a benign polyp.

six months. The patient exhibited typical signs of pyloric obstruction. On physical examination, she was dehydrated and appeared acutely ill. A distinct mass was palpated in the midabdomen at the level of the umbilicus. Her hemoglobin was 70 per cent, red blood count, 3,500,000. X-rays of the stomach revealed an extensive filling defect in the body and antrum. Increased peristalsis was visible and it was felt that there was an extensive carcinoma of the stomach, with involvement of the pyloric region (Fig. 16, Case 7). The patient was given a course of x-ray therapy with some improvement, but the attacks of epigastric pain and vomiting continued, so that sixteen days after admission it was decided to do a palliative gastroenterostomy. At operation the stomach wall was seen to be perfectly normal. A round movable mass was palpated, apparently attached to the posterior wall of the stomach. A large polypoid tumor was delivered through the anterior stomach wall, which had the gross appearance of a benign tumor and was found to be attached to the posterior wall of the stomach by a mucous membrane pedicle. The tumor appeared to have blocked the pylorus. It was excised locally. The postoperative course was smooth and the patient has been perfectly well since the operation.

Pathologic report.—The specimen consisted of a blood-red tumor mass measuring 6 by 4 by 3 cm., symmetrical and coarsely lobular. It was soft and friable and sections revealed innumerable glandular complexes. The cells lining the acini were regular, tall columnar, one layer thick. The surface of the tumor showed small, thin-walled blood vessels. Patches of hemorrhage, areas of ulceration and chronic

very slight provocation. The glands in the polyps are quite well formed (Fig. 14, Case 5).

Following operation, the patient was treated with dilute hydrochloric acid and liver, and discharged from the hospital, Sept. 1, 1935. She came to the outpatient department irregularly for about two years until April 13, 1939, when she was readmitted to the hospital with a true Addisonian anemia, the hemoglobin being 48 per cent, with 1,400,000 red blood cells. Roentgenologic examination of the stomach showed no evidence of recurrence of the polyp. The patient is being maintained on one vial (3 c.c.) of liver extract intramuscularly every three weeks.



Fig. 15 (Case 6).—Roentgenogram of stomach showing polypoid mass in the prepyloric area.

CASE 6.*—M. R. (New York Hospital No. 61150), a 54-year-old woman, was admitted April 9, 1934, with a complaint of weakness, numbness, and tingling of the toes, with some epigastric distress and belching. For the past twenty years, she has suffered from indigestion, gaseous distention, and vague abdominal pain. Three years ago she developed sore mouth, felt weak, and a gastric analysis revealed achlorhydria, while blood examinations revealed a profound anemia. Under intense liver therapy, she complained of weakness, lack of energy, numbness and tingling of the feet and hands. When liver therapy was stopped there was a tendency for the red blood cell count to drop. Her blood count on admission was 4,000,000, hemoglobin 88 per cent, with a slight variation in the size and shape of the red blood cells. Physical examination revealed a fairly well-developed and well-nourished woman. The papillae on the tongue were good. The abdomen appeared normal. Careful neurologic examination failed to reveal any abnormality. Roentgenologic examination of the gastrointestinal tract revealed a polypoid mass in the prepyloric area on the posterior wall, which was thought to be malignant (Fig. 15, Case 6). She left the hospital on April 25, 1934, to go home to Chicago where operation was to be considered by her family surgeon, who operated upon her in May, 1934. A pedunculated polyp was found near the pylorus on the posterior wall of the stomach. There were four other smaller polyps in this same region. These were excised locally on the assumption that they were benign, and frozen section showed no evidence of malignancy. Permanent sections were diagnosed as chronically inflamed adenomatous polyps, but very early malignancy could not be excluded with certainty.

Since operation her blood count has been maintained at a fairly normal level by liver therapy. She continues to have some abdominal distention and belching after meals. Follow-up x-rays of the stomach have been refused by the patient.

*Courtesy of Dr. Paul B. Sheldon.

CASE 8.—M. G. (New York Hospital No. 18984), a 52-year-old woman, was treated in the medical clinic from September, 1929, to July, 1931, for chronic constipation and an old paralysis of the tongue and right arm. Gastric analysis revealed no free hydrochloric acid. There was little change in her condition and she was treated at infrequent intervals in the medical clinic until June, 1939, when a gastric analysis again revealed an acidity. Fluoroscopic examination and films of the gastrointestinal tract showed a polyp on the posterior wall of the stomach in the region of the greater curvature (Fig. 18, Case 8). *She then was admitted to the hospital, where her hemoglobin was found to be 80 per cent and red blood cell count 4,000,000. On July*



Fig. 19 (Case 8).—Photomicrograph of benign polyp showing irregular large glandular structures lined with columnar epithelium.

27, 1939, operation revealed a small polyp about 2 cm. in diameter, easily palpated through the wall of the stomach in the lower portion of the pars media near the greater curvature. This appeared to lie on the anterior wall and was freely movable by virtue of a short pedicle. The remainder of the stomach and duodenum appeared quite normal. A linear incision was made into the stomach between traction sutures and the polyp transfixated through its loose pedicle, which contained only mucosa. The wound in the stomach was closed with mattress sutures of fine black silk.

Pathologic Report.—The specimen consisted of a pink, soft tumor measuring 8 by 9 by 5 mm. On section it was soft and whitish in color.

Microscopic.—Sections of this polyp showed its surface to be ulcerated and covered with purulent material. Immediately beneath this there was a very vascular inflamed fibrous tissue. The main body of the mass, however, was composed of irregular, large glandular structures lined with columnar epithelium. Most of these lining cells were goblet cells secreting mucus. In some areas, however, particularly near the surface, the cells stained more darkly and there appeared to be a few isolated strands which did not clearly form crypts. Amongst these there were fewer

inflammation were frequent. Examination of the base of the polyp showed it to be composed entirely of rather dense fibrous tissue which had few small blood vessels. There was no evidence of invasion of the base.

Diagnosis: Adenomatous polyp of the stomach (Fig. 17, Case 7).

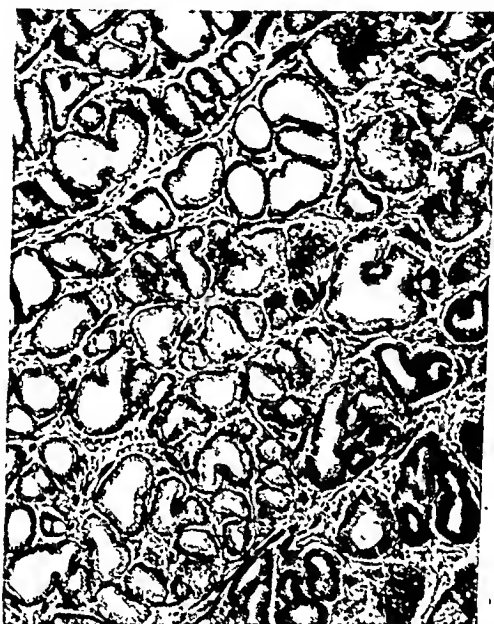


Fig. 17 (Case 7).—Photomicrograph of benign polyp showing innumerable glandular complexes. The cells lining the acini are regular, tall columnar, and one layer thick.



Fig. 18 (Case 8).—Punched-out, circumscribed defect in roentgenogram of stomach typical of benign polyp.

cm. from the pylorus. The tumor was locally excised and a posterior gastroenterostomy was done. Microscopic examination of the tumor showed it to be of unmistakable smooth muscle origin. Mitotic figures were not found and for this reason the tumor was classified as a nonmalignant leiomyoma of the stomach. The patient had an uneventful convalescence and was reported to be well nineteen months after operation.

REFERENCES

- Balfour, D. C., and Henderson, E. J.: Benign Tumors of the Stomach, *Ann. Surg.* 85: 354, 1927.
- Benedict, E. B., and Allen, A. W.: Adenomatous Polypi of the Stomach; With Special Reference to Malignant Degeneration, *Surg., Gynec. & Obst.* 58: 79, 1934.
- Conway, J. Herbert: Leiomyoma of the Stomach, *Arch. Surg.* 33: 792, 1936.
- Eliason, E. L., and Wright, V. W. M.: Benign Tumors of the Stomach, *Surg., Gynec. & Obst.* 41: 461, 1925.
- Gibson, C. L.: Ball-valve Tumor of the Stomach, *Ann. Surg.* 45: 130, 1907.
- Lahey, Frank H., and Colcock, B. P.: Diagnosis and Surgical Management of Leiomyomata and Leiomyosarcomata of the Stomach, *Ann. Surg.* 112: 671, 1940.
- Matas, R.: Pedunculated Polypoid Fibro-adenoma of the Stomach of Ball-valve Type, Causing an Unusual and Complex Syndrome, *Surg., Gynec. & Obst.* 37: 723, 1923.
- McRoberts, J. W.: Gastric Polyps, *Proc. Staff Meet., Mayo Clin.* 8: 685, 1933.
- Minnes, J. F., and Geschickter, C. F.: Benign Tumors of the Stomach, *Am. J. Cancer* 28: 136, 1936.
- Moore, A. B.: Benign Tumors of the Stomach From the Roentgenologic Point of View, *J. A. M. A.* 89: 368, 1927.

goblet cells. However, one could not consider this as a malignant change, particularly in view of the fact that the inflammation seemed more active about these areas. Close follow-up was advised (Fig. 19, Case 8).

Diagnosis: Gastric adenoma.

The patient did well after the operation and was discharged in about two weeks. She is being followed carefully in the outpatient department, with frequent examinations through the gastroscope. X-rays of the stomach Sept. 21, 1939, showed the rugal markings to be coarse. There was a smooth indentation on the greater curvature on the pyloric end. There were no defects and no evidence of polyp (Fig. 20, Case 8). The last gastroscopic examination, three years after operation, revealed two small sessile polyps less than 1 cm. in diameter. One was near the



FIG. 20 (Case 8).—Postoperative x-ray film of stomach showing no defects and no evidence of polyp.

angularis on the lesser curvature and the other opposite this on the greater curvature. The pyloric ring appeared to be normal. At the last clinic visit in April, 1941, the patient reported that she was working but that she had some epigastric pain and distress. Gastric analysis again revealed no free hydrochloric acid. Hemoglobin was 88 per cent, red blood cell count, 4,200,000.

CASE 9.—This was the one leiomyoma of the entire group. It has already been reported in detail by Conway, in 1936.

F. S. (New York Hospital No. 76807), male, aged 41 years, was admitted to the surgical service Oct. 5, 1934, in a state of shock after sudden hematemesis. Following appropriate therapy, he slowly recovered from the profound anemia. Serial roentgenograms of the gastrointestinal tract on two occasions showed nothing abnormal in the stomach and duodenum. Operation Nov. 15, 1934, revealed a small tumor measuring 2 by 2 cm. in the wall of the lesser curvature of the stomach, 6

two groups, experimental and control. The former were given heparin intraperitoneally at the close of the operation and in varying dosages by abdominal paracentesis thereafter. A series of dosage experiments, previously reported,² indicated that for full effect heparin must be given for at least three days after separation of adhesions, and all of the experiments reported are from animals so treated. The control group was further subdivided. One subgroup received no auxiliary treatment, and one subgroup each was treated with corresponding amounts of normal saline solution, amniotic fluid^e and papain solution.[†] After a further period of two to six weeks, at a third laparotomy, the number and extent of re-formed adhesions were recorded. In a series of ten experiments, repeated division of adhesions followed by heparin administration was carried out in individual animals.

RESULTS

The results (Fig. 1) have been remarkably consistent throughout. It is clear that under the described conditions of experimentation, heparin has proved considerably more effective in the dog than any other agent. In the controls more adhesions re-form than are divided even with the use of such drugs as amniotic fluid and papain, which seem to possess no advantageous action. With the use of heparin, however, the average re-formation rate is only 35 per cent of the number divided.

The gross data were broken down in an attempt to determine whether the number of adhesions divided influenced the percentage result. Those heparin animals in which six or more adhesions were divided presented approximately the same percentage of recurrence as those with fewer adhesions.[‡]

In the earlier portion of the study heparin from the Connaught Laboratories was employed exclusively. After extensive testing on blood coagulation both in vitro and in vivo, we later shifted to Liquaemin, a domestic heparin.[§] The preliminary studies indicated almost equal effectiveness and equal nontoxicity of the two products. When the results of intraperitoneal employment were divided according to the product used (Fig. 2), there was a slight difference in favor of the Connaught material which averaged 30.7 per cent of re-formation as compared to 41 per cent in a smaller series of Liquaemin experiments. This difference is believed to be within the limits of error of the necessarily crude method of quantitative measurement, although it corresponds roughly to the differences observed in the effect on blood coagulation of the two products.

The results of repeated division of adhesions indicate that with the use of heparin progressive diminution of the number occurs. When the

*Amfetin, supplied by Eli Lilly and Company.

†Supplied by Parke-Davis & Co.

‡This statement takes precedence over the statement of Boys (reference 4, p. 144) which was made on calculations from a smaller number of observations.

§Furnished by the courtesy of Hoffmann-LaRoche, Inc.

EXPERIMENTAL PREVENTION OF INTRAPERITONEAL ADHESIONS WITH HEPARIN

THIRD REPORT*

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WE PUBLISHED, in 1940, two preliminary papers on the effect of heparin in the prevention of the reformation of experimentally produced peritoneal adhesions.^{1, 2} The reported studies included experiments and control observations on fifty-six dogs, indicating an unmistakably favorable effect of heparin. The rationale of the methods and its attendant dangers were fully discussed.

The present report deals with additional experimental work. After the publication of the last paper the entire subject was reopened in the laboratory and restudied with greatly enlarged experimental and control series. This step seemed important because of the danger that more skillful operative handling of adhesions with added experience might have weighted the results in favor of heparin. The new experiments total twice as many as those previously reported. The present paper, recording more than 170 experiments, consolidates the older material with the later results.

METHODS

At the start of the investigation, clinical conditions were mimicked in the production of peritoneal adhesions by creating an infectious peritonitis from fecal contamination caused by an intraperitoneal appendicostomy. The mortality from this procedure due to acute suppurative peritonitis was about 50 per cent; this wastage of animals was later avoided by employing mechanical damage to create adhesions. As the results of the two methods are approximately the same, no attempt will be made to divide the experiments reported according to the etiology of the adhesions. About six weeks after the operation to create adhesions (either by contamination or scarification), the abdomen was reopened, the adhesions counted and, in the latter half of the study, also measured. Complete separation of all adhesions was then carried out largely by sharp dissection. After effecting complete hemostasis, the abdomen was closed. At this stage the animals were divided into

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DISCUSSION

Although there have been rare individual failures of heparin effect in the course of this study, the average results including such failures have been remarkably uniform. The data reported above seem to indicate that heparin is unquestionably effective in the dog in diminishing the number of adhesions re-formed following division.

The results of this study strongly indicate the possibility that heparin may be made to play a role in the process of inflammation, particularly in its later stages. The prevention of fibrin formation in an exudate by heparin may modify the production of granulation tissue. The implications of this possible mechanism are twofold. In the first place, as in the present experiments, the result may be a quantitative diminution of scar tissue. From this point of view the method may be practically applicable to many conditions in which scar tissue creates a diseased state in itself. As previously suggested,¹ such conditions include adhesions within joints, tendon sheaths, and the pericardium as well as the peritoneum.

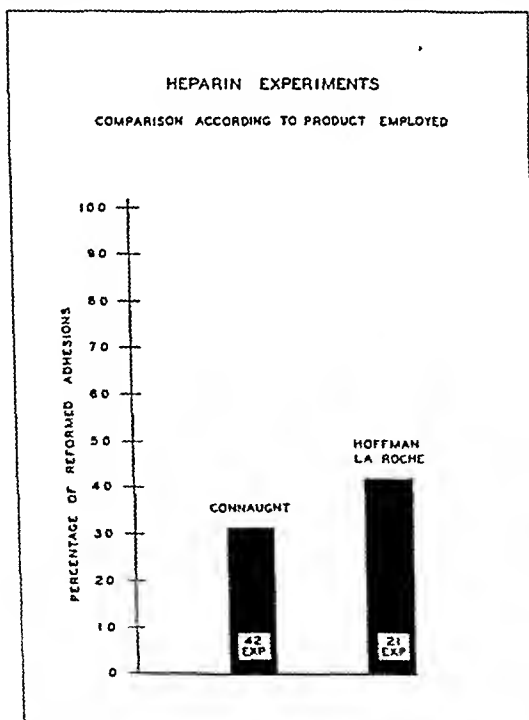


Fig. 2.—Comparison of the effectiveness of two brands of heparin in the prevention of the re-formation of divided adhesions. The difference shown is probably within the limit of error of the method of measurement.

In the second place, the prevention of the development of granulation tissue which is a constant accompaniment of the healing stage of advanced inflammatory processes implies the retardation of recovery.

original heparin animals were subjected to a second division of adhesions followed by heparin treatment, the final number of re-formed adhesions was only 24 per cent of the number at the beginning of the experiment as compared to 168 per cent in controls (Fig. 3). In three of the ten heparinized animals the abdomen was completely free of adhesions, in one instance when ten adhesions had been originally divided. In three other instances, only one adhesion remained and in two instances only two. With the omission of the only unfavorable experiment in this group, the average final re-formation rate for the remaining nine was 17 per cent.

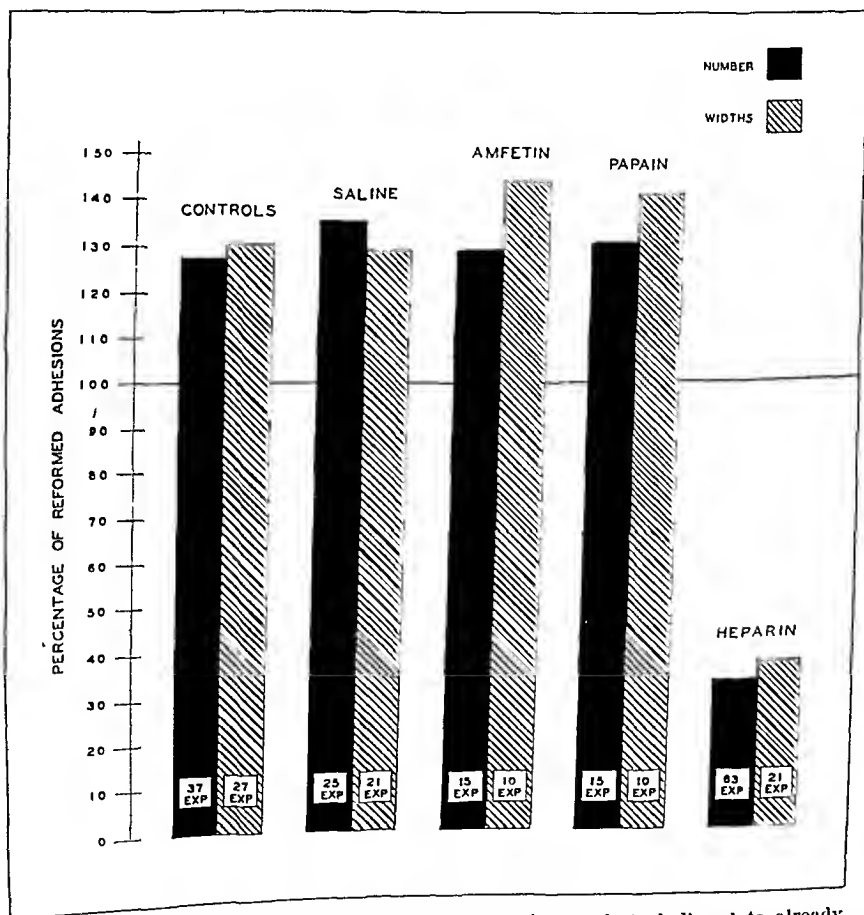


Fig. 1.—Consolidated results of all experiments and controls including data already published.^{1,2} Three-quarters of the data presented here are new. The blocks represent the average percentage re-formation rate of divided adhesions.

Since especial care has been taken with hemostasis, hemorrhage has ceased to be an experimental hazard. There have been as many as 101 consecutive intraperitoneal applications of heparin after the division of adhesions without bleeding.

CONCLUSIONS

1. Heparin administered intraperitoneally definitely diminishes the re-formation rate of divided adhesions in the experimental animal.
2. The extension of the principle to other structures in which fibrosis may be harmful is suggested.
3. The clinical application of the method in the peritoneal cavity is justified under indications and contraindications discussed elsewhere.

REFERENCES

1. Lehman, E. P., and Boys, F.: The Prevention of Peritoneal Adhesions With Heparin, *Ann. Surg.* 111: 427-437, 1940.
2. Lehman, E. P., and Boys, F.: Heparin in the Prevention of Peritoneal Adhesions, *Ann. Surg.* 112: 969-974, 1940.
3. Lehman, E. P., and Boys, F.: Clinical Use of Heparin in the Peritoneum for the Prevention of Adhesions. Report of Fourteen Cases, *Arch. Surg.* 43: 933-945, 1941.
4. Boys, F.: The Prophylaxis of Peritoneal Adhesions, *SURGERY* 11: 118-168, 1942.

Careful quantitative studies are needed to determine whether wound healing is retarded and whether infections are prolonged by the exhibition of heparin.

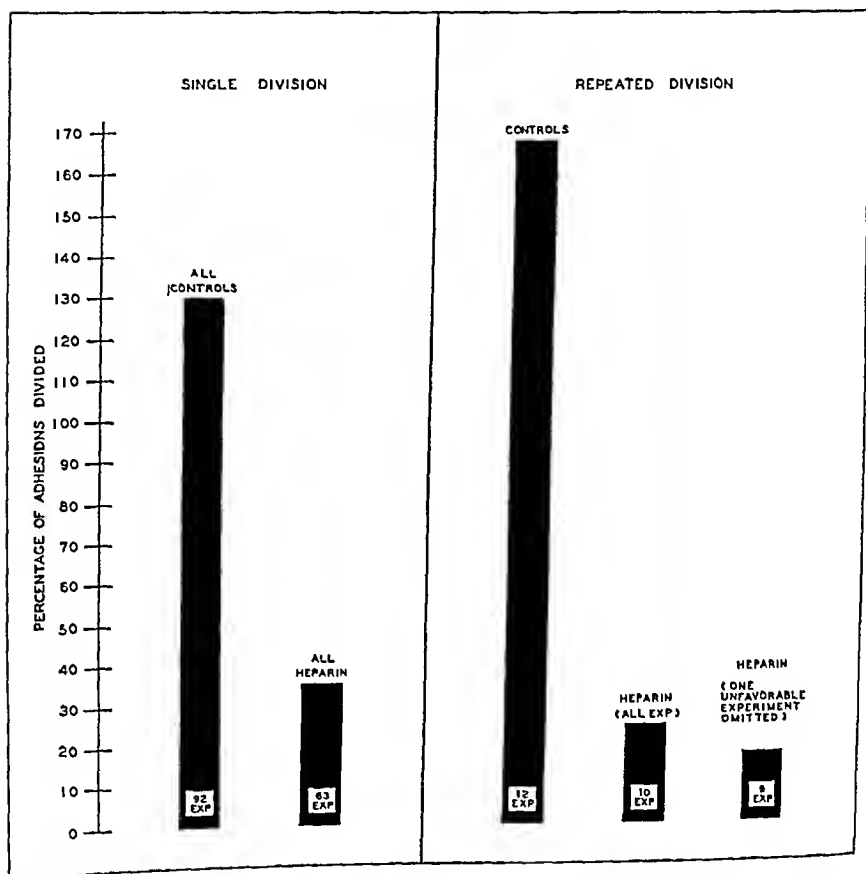


Fig. 3.—Comparison of the re-formation rate following repeated division of adhesions with and without intraperitoneal heparin administration.

Finally, the experimental results recorded above are so striking and the one danger of the method, namely hemorrhage, is so clearly defined, that the clinical application of the principle in the prevention of peritoneal adhesions is now considered justified. A recent report³ presents the results of intraperitoneal heparinization in fourteen clinical cases. Since the preparation of that report there have been several other cases without complications. Of the fourteen cases reported, one patient died of intraperitoneal hemorrhage as the result of unmistakably improper choice of case coupled with imperfect postoperative observation. For details of the clinical application including the indications, the contraindications, the technique, and the precautions, it is urged that the clinical report referred to³ be consulted.

and subsequent doses of 0.25 Gm. per kilogram of body weight per day. This drug was also begun three days preoperatively and continued until sacrifice. The blood levels of the dogs were determined by the method of Marshall and Cutting⁴ on the day of operation and on the day they were sacrificed. The control animals received no sulfonamides.

Sixteen dogs were used in the experimental group in the sulfanilamide studies. The animals were sacrificed at selected postoperative intervals, namely four, five, six, seven, eight, nine, ten, eleven, twelve, and thirteen days postoperatively. In the sulfadiazine studies there were fifteen animals in the experimental group. These were sacrificed on the third, fifth, seventh, ninth, eleventh and thirteenth postoperative days. The control group consisted of sixteen dogs sacrificed postoperatively at intervals of three, four, five, seven, eight, nine, eleven, and thirteen days. The sulfanilamide, sulfadiazine, and control animals were all subjected to the same operative technique.

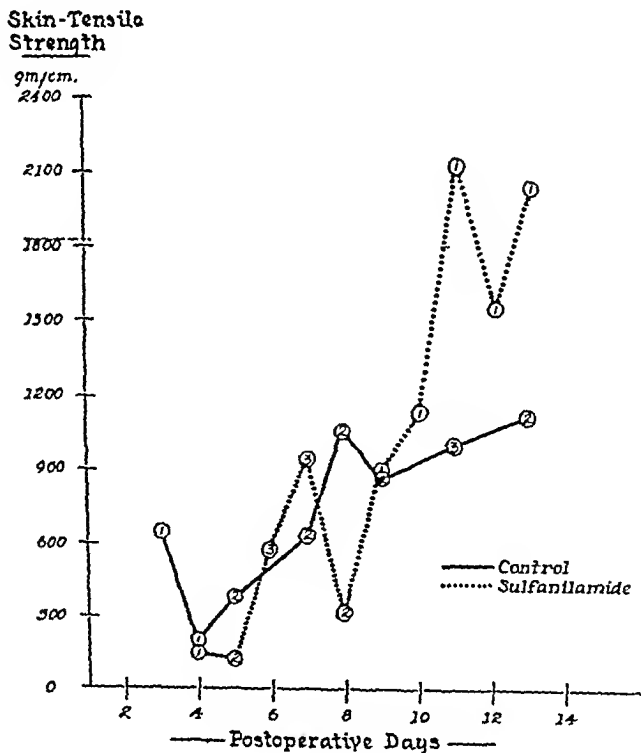


FIG. 1.

The skin of the right upper abdominal quadrant was used for these studies. Under aseptic technique a transverse incision about 2 cm. in length was made through the skin at this site. After careful hemostasis the incision was promptly closed with fine silk interrupted sutures.

EFFECT OF THERAPEUTIC BLOOD LEVELS OF SULFANILAMIDE AND SULFADIAZINE ON WOUND HEALING

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THE extensive use of the sulfonamides to prevent and control infection in surgical wounds has raised the question of the possible effect that these drugs may have on wound healing. Several papers have already been published on this subject. It seemed that with the widespread use of these compounds in civil and military practice, and with the differences in opinion which have arisen, the subject might be investigated further under different environmental conditions. We have studied the tensile strength of healing wounds in dogs receiving sulfanilamide and sulfadiazine.

METHOD

Mongrel dogs were selected as the experimental animals. The tensile strength of the wounds and histologic studies were used as the indices of healing. Skin, fascia, and stomach wall were the tissues which were studied. Since hypoproteinemia impairs wound healing, as has been shown by Thompson, Ravdin, and Frank,¹ serum protein concentrations were determined at operation and at the time the dogs were sacrificed, using the method of Barbour and Hamilton.² It should be mentioned that the normal serum protein level of dogs is somewhat lower than that of man, being about 6.0 Gm. per cent.

An adequate intake of vitamin C is also necessary for normal wound healing (Lanman and Ingalls³). This was insured by giving all the animals throughout the experiment a diet ample for all nutritional needs, and in addition, those animals receiving chemotherapy were given 10 mg. of ascorbic acid daily with their sulfonamide drug. The animals were weighed at the time of operation and again at the time they were sacrificed.

Adequate therapeutic drug levels were maintained in the experimental group of animals by the administration of the sulfonamides directly into the stomach by means of a stomach tube. In the case of the sulfanilamide group, sulfanilamide powder in dosages of 3.0 Gm. daily were given in three divided doses, eight hours apart. The drug was begun three days preoperatively and continued daily until the animal was sacrificed. The sulfadiazine dogs were given an initial dose of 0.5 Gm.

No dressing was applied. On the day of sacrifice, the skin sutures were removed and an area two inches square was measured around this incision. This area of skin was dissected free from the underlying subcutaneous tissue, pinned on a wooden block to its original size and shape, and a piece of the tissue including 1 cm. of the wound was stamped from the square by means of a steel die. The tensile strength of this piece of tissue was measured by the tensiometer method of Meade.⁵ This method provides a measure of the number of grams required to disrupt an area of the wound 1 cm. in cross section. Histologic sections were prepared from a separate section of the wound.

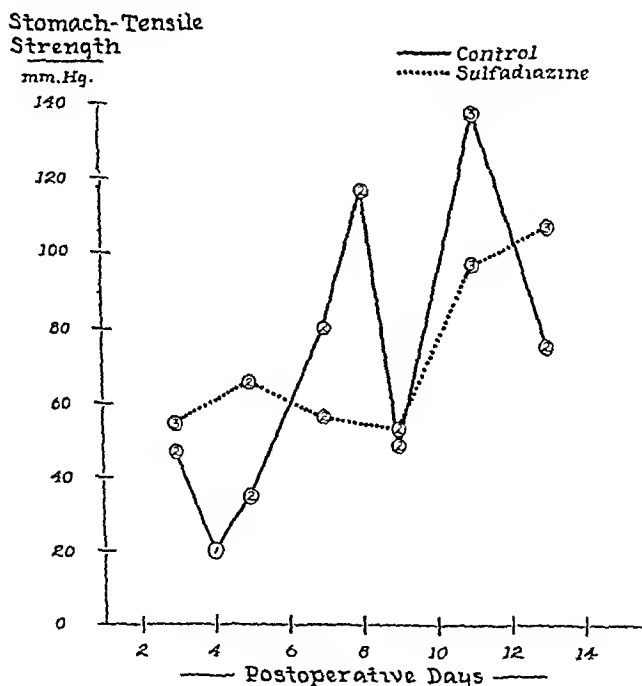


FIG. 4.

The stomach was approached through a midline abdominal incision. After exposure of the stomach an intestinal clamp was applied, and an incision exactly 2 cm. in length was made through the anterior wall of the cardia. Care was taken to avoid the larger vessels. The incision was promptly closed with two layers of interrupted plain 000 catgut. The first layer included mucosa and submucosa, and the second included muscularis and serosa. Care was used to make certain that there was no bleeding from the wound after the gastric clamp had been removed. The peritoneum, fascia, and skin of the abdominal incision were closed by means of fine continuous silk sutures. On the day of sacrifice the stomach was removed, and the tensile strength of the

Skin-Tensile Strength

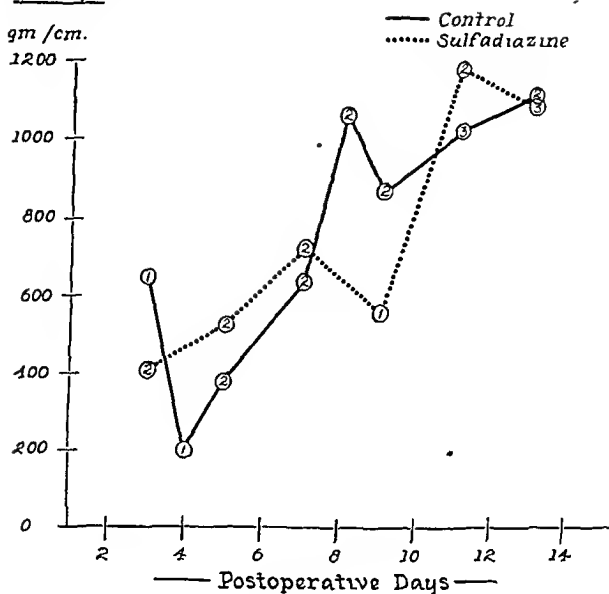


Fig. 2.

Stomach-Tensile Strength

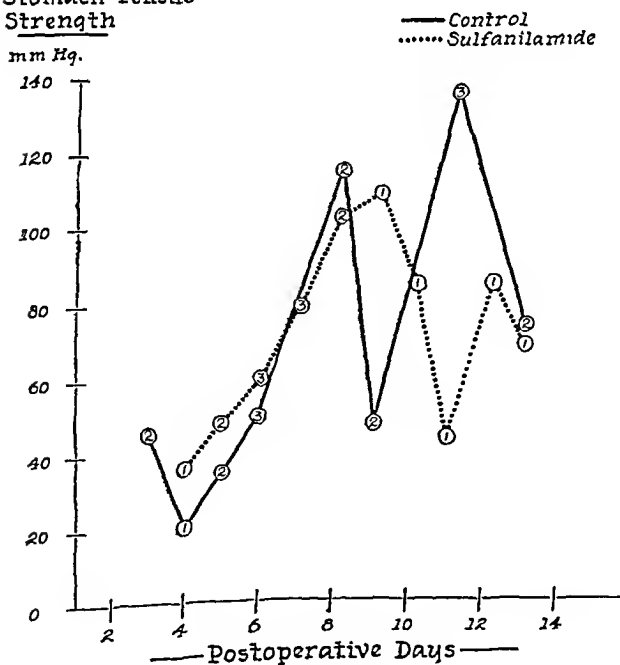


FIG. 3.

wound was then determined by the air pressure inflation mercury manometer method of Harvey and Howes.⁶ Histologic sections were also made of these wounds.

The upper third of the left anterior rectus sheath was exposed and a transverse incision approximately 2 cm. in length was made through it and promptly closed with plain 0 catgut by interrupted sutures. Careful hemostasis was observed. On the day of sacrifice an area two inches square was measured around the wound site. This area of fascia was dissected free from the underlying muscle and the tensile strength measured in the same manner as that of the skin. Histologic sections were made of the wound site.



Fig 7—Control dog, No 337. Photomicrograph of section through stomach incision eleven days postoperatively. Complete repair of mucosa can be seen. Muscular layers are healed by fibroblastic proliferation.

The operations were performed under either sodium amytal anesthesia, 50 mg. per kilogram of body weight administered intraperitoneally, or by the open-drop ether method. An aseptic technique was employed for all operations and care was used to obtain perfect hemostasis. Trauma was minimized. The animals were sacrificed by giving an intracardial injection of chloroform. Careful handling of the wound

Fascia-Tensile Strength

gm./cm

2100

1800

1500

1200

900

600

300

0

— Control

..... Sulfanilamide

— Postoperative Days —

Fig. 5.

Fascia-Tensile Strength

gm./cm

2100

1800

1500

1200

900

600

300

0

— Control

..... Sulfadiazine

— Postoperative Days —

Fig. 6.

of polymorphonuclear leucocytes, fibrin, and detritis. This was due partly to the trauma of operation and partly to postoperative trauma as no dressings were used. The extent of epithelization varied somewhat in different dogs in both the experimental and the control groups on comparable days.

The results of the tensile strength studies of the stomach are expressed in millimeters of mercury and no significant differences were found between those animals receiving sulfonamide and those used as controls. Little difference was found on histologic examination of the wounds in the dogs receiving sulfonamide and in the control dogs of comparable postoperative days (Figs. 7 and 8). Mucosal regeneration was, as a rule, complete in both sets of dogs from the seventh day. The submucosa, muscularis, and serosa were also fairly well healed by fibroblastic proliferation at that time. There was no evidence of inflammatory reaction, edema, or hematoma.

The tensile strength figures for fascial tissue in control wounds closely paralleled those of the sulfonamide wounds. Microscopically the healing appeared the same in both groups of animals. Inflammatory changes were not seen as often in these sections as in the skin group. This is accounted for largely by the fact that the skin wound was exposed to external bacteria and trauma during the healing period.

In all six graphs there can be seen occasional wide variations in both directions from the general trend of the curves. These variations are seen in both control and experimental animals and have been noticed and commented upon in studies made by other workers.¹⁰

The sulfanilamide concentration varied in the treated group between 2.3 and 30.8 mg. per cent, with an average of 19.7 mg. per cent of those levels taken approximately eight hours after the last administration of the drug. The sulfadiazine levels were between 6.7 and 36.4 mg. per cent, with an average of 17.7 mg. per cent. The specimens for sulfadiazine levels were taken approximately twenty-four hours after the last drug administration.

The body weight of the dogs was satisfactorily maintained and only two of the forty-nine dogs had serum protein concentrations below normal, both of these being 4.7 Gm. per cent. Neither one of these two animals showed significant variations from the final tensile strength curves.

DISCUSSION

Our results seem to indicate that sulfanilamide and sulfadiazine in adequate concentrations in the tissue fluids do not retard or inhibit wound healing. The curves of healing of the control animals as compared to those of the experimental groups are practically identical and histologic studies revealed no striking differences. This is true of skin, fascia, and stomach wall in dogs.

tissue during the manipulations necessary for tensile strength determinations was used to avoid any artificial disruption of the wounds.



Fig. 8.—Dog No. 277, given sulfadiazine. Photomicrograph of section through stomach incision eleven days postoperatively. Complete repair of mucosa can be seen. Muscular layers are healed by fibroblastic proliferation.

RESULTS

As shown in Figs. 1 to 6, there was found to be no appreciable difference between the tensile strength of the skin wounds in those animals receiving sulfanilamide and sulfadiazine, from those of the control group. Wherever possible, two or more dogs were used to determine the average for each day of sacrifice. It should be pointed out that our tensile strength figures are a little lower through the experiment than those given by other methods because we stretched the skin to its original size and shape before cutting the specimen. Other workers have not done this, allowing the tissue to contract before cutting the specimen, and thus including more actual tissue in their specimen than we did. Histologic studies of some of these skin wounds showed some inflammatory reaction of varying degrees as evidenced by the presence

A STUDY OF THE PHYSICAL FACTORS CONCERNED IN INFLAMMATION

I. THE ROLE OF HYDROSTATIC AND PHYSICOCHEMICAL FORCES IN THE ESTABLISHMENT OF CERTAIN EQUILIBRIA*

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INTRODUCTION

General Definition of the Inflammatory Process

ADAMI² has characterized inflammation as the reaction of irritated or damaged tissues which still retain vitality, being essentially a process of adaptation of the organism. It consists of a series of changes locally manifesting the attempt at repair of actual or referred injury to a part. Cohnheim²¹ considered inflammation as a process to reduce the harmful consequences of injury, and Opie⁴⁷ defined inflammation as a process by means of which cells and serum accumulate about an injurious substance and tend to remove or destroy it. Excellent descriptions of the inflammatory process have been recorded, and each observer has attempted to rationalize the clinical and microscopic appearance of the inflamed tissues on the basis of the underlying histology. Virchow emphasized that the increased metabolism of the inflamed area was due to the increased nutritive demands of the involved tissues.

Capillaries in inflammation.—William Harvey³⁵ noted the many circumstances which altered the blood flow, and Burke attempted to explain the inflammatory process primarily as a result of capillary dilatation. Using a plethysmograph with photographic recording, Burton¹⁶ showed that from full constriction to full dilatation there was an increase from 5 c.c. per min. per 100 Gm. tissue to 60 c.c. per min. per 100 Gm. tissue.

After Bayless and Gaskell²² had shown that carbon dioxide is a capillary dilator, Findlay²⁹ stated that histamine-like substances liberated at the point of injury caused a local dilatation of the small vessels and arterioles and an increased permeability of the local vessel walls. This same conception has been held by others (Dale and co-workers²³), and Harris showed that vasodilatation in the submaxillary gland may be produced by the collection of metabolites and that the production of osmotically active substances greatly increased filtration.

Although Rieker and Regendanz²² had maintained that the capillaries in inflammation are not more permeable and that the composition of the edema fluid could be explained by increased intracapillary pressure,

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An early report by Brieker and Graham⁹ on the effect of oral administration of sulfanilamide on the stomach wall of dogs at the third, fifth, and seventh postoperative days seemed to indicate that this drug had an inhibiting effect on wound healing. Their experiments did not extend over all the phases of wound healing, going up only to the seventh postoperative day. Taffel and Harvey,⁷ working with the same drug and studying gastric wounds in rats, found no change in the rate of healing.

Key, Frankel, and Burford,⁸ using local sulfanilamide implantation in muscle, fascia, and subcutaneous tissue of dogs, obtained findings similar to our own. Recently Harbison and Key,¹⁰ using sulfanilamide, sulfathiazole, and sulfadiazine implanted locally in wounds in rats, found no significant retardation of healing.

Our findings confirm and extend the observations of recent workers in this field who have shown that sulfonamides have no inhibiting effect on wound healing, when adequate concentrations in the blood are maintained and when eaking in the wound is prevented.

CONCLUSIONS

1. Sixteen dogs fed sulfanilamide by intubation and sixteen control dogs were studied from the standpoint of tensile strength and histologic picture of surgical wounds made in the stomach wall, the fascia, and the skin at four-, five-, six-, seven-, eight-, nine-, ten-, eleven-, twelve-, and thirteen-day intervals. No appreciable difference was found.

2. Fifteen dogs fed sulfadiazine were studied in a similar manner at the third, fifth, seventh, ninth, eleventh, and thirteenth postoperative days and no significant difference was found.

3. Therapeutic sulfanilamide and sulfadiazine blood levels do not inhibit wound healing.

REFERENCES

1. Thompson, W. D., Ravdin, I. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption, *Arch. Surg.* 36: 500, 1938.
2. Barbour, H. S., and Hamilton, W. F.: The Falling Drop for Determining Specific Gravity, *J. Biol. Chem.* 69: 625, 1926.
3. Lanman, T. H., and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing, *Ann. Surg.* 105: 616, 1937.
4. Marshall, E. K., Jr., and Cutting, W. C.: Absorption and Excretion of Sulfanilamide in the Mouse and Rat, *Bull. Johns Hopkins Hosp.* 63: 328, 1938.
5. Meade, R. H.: The Tensile Strength of the Paralyzed Diaphragm, *J. Thoracic Surg.* 2: 503, 1933.
6. Harvey, S. C., and Howes, E. L.: Effect of High Protein Diet on the Velocity of Growth of Fibroblasts in the Healing Wound, *Ann. Surg.* 91: 641, 1930.
7. Taffel, M., and Harvey, S. C.: Effect of Sulfanilamide on Wound Healing, *Proc. Soc. Exper. Biol. & Med.* 45: 647, 1940.
8. Key, J. A., Frankel, C. J., and Burford, T. H.: The Local Use of Sulfanilamide in Varicose Tissues, *J. Bone & Joint Surg.* 22: 952, 1940.
9. Brieker, E. M., and Graham, E. A.: The Inhibitory Effect of Sulfanilamide on Wound Healing, *J. A. M. A.* 112: 2593, 1939.
10. Harbison, S. P., and Key, J. A.: Local Implantation of Sulfanilamide and Its Derivatives in Wounds, *Arch. Surg.* 44: 22, 1942.

(Drinker and Field;²⁵ Coneklin;²² R. Magnus;⁴² Churchill, Hakazawa, and Drinker;¹⁰ Peters;⁴⁹ and Böhm¹²).

Lymph formation and the character of exudates have received considerable treatment in the literature, and Meyer⁴⁵ has adequately discussed the origin and removal of edema fluid. It is generally conceded that subcutaneous lymph and plasma are nearly identical in chemical composition except for proteins and substances (phosphorus and calcium) combined with protein (Underhill and co-workers;⁶² and Drinker and Field²⁵). Subcutaneous lymph in the human being has been found to contain as high as 3.5 per cent protein, the albumin-globulin ratio being the same as that in the corresponding blood plasma.

The fibrinogen content of blood plasma in acute infections is markedly increased and this may account for the gelatinous matrix of the inflammatory field. This exudate, when rendered cell free, is far more bactericidal than is the blood serum of the same animal, but it appears that leucocytic products are largely responsible for this activity.

Regional Lymph Flow

In the horse, a volume of lymph equal to that of the blood may be obtained in twenty-four hours. Starling⁵⁷ showed that in order to get any lymph at all for study in the normal animal, one has to knead or passively move the limb. This probably increases the protein content so that "normal" figures are inaccurate. In edematous tissues, however, the connective tissue tends to hold the lymphatics open so that there is a greater lymph flow, the oncotic pressure of the blood opposing the capillary filtration pressure. Exercise, heat, and inflammation increase the lymph flow and pressure (McMaster and collaborators⁴³), and, in fact, if mildly inflamed, lymphatics will allow the diffusion of otherwise indiffusible dyes through their walls.

From a clinical standpoint, it is interesting that Parsons and McMaster discovered that pulsatile perfusion of rabbit ear blood vessels caused fifteen to twenty times more rapid lymph flow than when constant blood pressure was applied, despite the fact that in many instances less blood flow per gram of ear occurred. Edema sometimes developed during the course of a pulsatile transfusion, concurrent with an enormous increase of lymph flow, although the volume of blood perfused was relatively small.

Statement of the Problem

Although the sulfonamides at present begin to hold out some hope in the stemming of spreading infection, there has yet appeared no immunologic agent to burden the surgeon of his struggle with this type of condition. As Wangenstein⁷ has pointed out, the surgeon has learned that incision of extending areas of phlegmon and cellulitis does not stem the spread of infection, that, in fact, such procedures do harm. Whether such an infection be in the soft tissues of the arm, leg, brain, or lung, the surgeon must restrain himself and support the natural

other observers insist that the capillaries are rendered highly permeable during inflammation. Still other investigators have explained the apparent increased permeability as being due to capillary stasis and opening of arteriovenous anastomoses (Clark and Clark²⁰) with establishment of a greater capillary bed.

The papers of Sir Thomas Lewis⁴⁰ record his experiments on capillary reactivity, particularly as regards wheal formation. In his words, "... there exists in the skin a single and organized mechanism of defense against injury of all kinds and . . . the agent which alarms the garrison and mobilizes the first forces of this defense is a chemical agent derived from the tissues . . . being independent of higher centers of organization (nervous) and of distribution (vaseular)."

Diapedesis.—With the dilatation of capillaries in the inflammatory field and the resulting slowing of the stream, margination and emigration are coincident phenomena. Arnold⁴ insisted that diapedesis took place through preformed stomata in the capillary wall. The French school strongly believed in diapedesis as an active process induced by contact of the capillary wall with bacteria or their products. Fischer³⁰ led a school which did not believe in capillary stomata. He showed that erythrocytes could pass through gelatin by gravity or pressure without leaving holes or any other traces, just as mercury will pass through solidified gelatin.

Abramson¹ was probably the first to investigate the intimate relationships between electrostatic charges on the blood cell surfaces and that on the capillary walls. Although it had been known for a long time that dead or living bacteria or their products were strongly chemiotactic, it was not until the studies of Falk and his co-workers²⁸ that the electrophoretic potential of bacteria and leucocytes was quantitated.

The brilliant papers of Abramson on the alteration of electrostatic charge induced by inflammation should be reviewed by every student of the subject. Briefly, it appears that normally blood cells (Bellis and Scott¹⁰) and capillary membranes possess a negative charge (thermodynamic and electrokinetic potentials). In inflammation, the potential on the capillary is reduced causing attraction of leucocytes (margination), diapedesis resulting from the increased potential difference between the colloidal micelles in the tissue spaces and the leucocytes. Both the thermodynamic and electrokinetic potentials on the leucocyte are greater than on the erythrocyte because of the greater size of the leucocyte; hence, a much greater reduction of potential on the capillary is necessary to produce a margination and migration of erythrocytes. In severe inflammations even this takes place.

Permeability of Capillaries to Protein

Although the glomerular ultrafiltrate is normally protein free, the capillary wall in other parts of the body is permeable to protein

Heat aggravates filtration through both normally and abnormally permeable capillaries, and therefore the temperature of the skin should be a reflection, in part, of the amount and rate of capillary filtration and swelling. Therefore, skin surface temperatures were measured in normal extremities and in many types of inflammations. At the same time, the abnormal capillary permeability was studied by determining the specific gravity and protein content of the edema fluid.

Having made these clinical observations, it was determined to alter and control the conditions in the experimental animal, to establish, if possible, a predictable basis for evaluating certain of the factors. It was proposed to determine, in the same animal, the oncotic pressure exerted by the blood on one hand and the tissue fluid on the other, as well as the capillary filtration pressure and the resistance of the tissues to distention. Special observations were intended of the volume changes occurring in experimentally inflamed extremities, the pH of the edema fluid, and the relation of the edema fluid protein concentration to plasma protein concentration. The rate of lymph flow in the lymphatics draining an inflamed area should be different from that draining a normal area and it was planned to study the rate of this flow.

Finally, the results obtained by immobilization and elevation of inflamed extremities were evaluated by a questionnaire sent to a large series of patients so treated.

METHODS AND EXPERIMENTS

Position and Blood Flow in the Patient

Arterial Blood Pressure.—In twelve individuals the radial systolic blood pressure was determined with the arm (1) horizontal, that is, in the plane of the horizontally lying individual; (2) elevated perpendicular to the body; and (3) dependent perpendicular to the body over the side of the bed. These results were then tabulated.

Skin Surface Temperatures.—The skin surface temperatures of a finger in each of five normal individuals were determined in the horizontal position and after one hour of elevation perpendicular to the horizontal, using the apparatus of Bellis and Cook.⁹

In each of six men, the skin surface temperatures along both lower extremities were determined with both extremities in the plane of the horizontal trunk, and after having maintained the right lower extremity elevated for about twelve hours at an angle of 60°. The skin surface temperatures of another individual were determined before and after twelve hours in semi-Fowler's position.

Tissue Tensions in the Patient

Normal Tissue Tensions.—Landerer¹⁰ appears to have been the first to consider the importance of tissue elasticity or tension in counterbalancing capillary filtration. He used a direct manometric system with a

defenses of the body, withholding actual surgical intervention until signs of localized suppuration are evident. Then, and only then, should incision and drainage be established.

Formerly, therapy was direct at reduction of the effects of inflammation, but more recently it was suggested by some pathologists that the accompanying swelling was useful and helped fix the infection locally and lessened the tendency to centripetal spread. A boil, so to speak, was small price to pay for protection from pyemia. Mindful of this Bier¹¹ sought to increase the heat and swelling attending infection by application of heat, by obstructing the venous return, and by cupping. Noetzel believed that there is a current of tissue fluid established by Bier's hyperemia, the new transudate being bactericidal and the hyperemia stimulating fibrosis.

Undoubtedly, inflammatory exudate possesses immunologic properties; yet, the impression cannot be avoided that tense edema is harmful, the factor limiting the transudation being the distensibility of the tissues. It has been observed clinically that elevation, immobilization, and avoidance of heat accelerate the clearing up of infection and are accompanied by striking relief of pain.

The stimulation to investigate the underlying physical factors in inflammation came from these clear-cut clinical observations, and an attempt was made to correlate these factors with the treatment. It was expected that exact quantitation of certain values would not be possible, nor would all the factors be known. However, it was necessary that certain quantitative as well as qualitative data (as observed in the clinic) be obtained under experimental control.

To this end, the relation between position of an extremity and the systolic blood pressure distally was determined, since elevation is known to reduce the hydrostatic force of the systolic blood pressure in direct ratio to the degree of elevation of the part. What effect elevation has on the systolic pressure should be reflected in the skin surface temperatures. It was, therefore, proposed to measure these temperatures in the horizontal position and after elevation of the extremity.

Tissue swelling occurs through the agency of increased capillary permeability and intracapillary pressure. The increasing tissue pressure causes venous compression and augmented venous pressure with a further increase in intracapillary pressure. This cycle augments further filtration of fluid into the inflamed area. It was obvious that in order to evaluate the effects of tissue tension, normal tissue tensions and then the tensions at inflammatory sites had to be determined.

Having obtained information as to the relation of position to blood flow and the degree of tissue pressure exerted in inflammation, it followed that the volume of the inflamed extremity must be increased over that of the normal. The very effect of gravity on a normal extremity was questioned and studied and the volume differences in various types of inflammations were measured.

cases the pressures were determined before immobilization, and in 22 cases the intramuscular pressures were determined after partial immobilization. The pressures were also obtained in a shorter series of miscellaneous affections.

In a series of twenty cases of inflammations involving either an upper or lower extremity in which the skin surface temperatures were also measured, the tissue tensions at several corresponding points in the affected and unaffected extremities were determined.

Position and Volume Changes in the Human Being

It has been known for a long time that quiet standing leads to hemoconcentration, manifested by an increase in the specific gravity of the blood and plasma and decrease in circulating blood volume (Böhme;¹³ Harrop and Waterfield;³⁴ Thompson, Thompson, and Daily;⁶⁰ and Yonmans⁶⁷). Venous congestion has been shown to have a similar effect (Rowe,⁵⁴ Plass and Rourke,⁵⁰ and Reiss⁵¹).

It is not surprising, therefore, that attention has been directed by many observers to the increase in volume of an extremity when it is dependent or when the venous return is partly or entirely occluded (Atzler and Herbst,⁵ Stead and Kunkel,⁵⁸ Wells,⁶⁵ Waterfield,⁶⁴ Mende,⁴⁴ White and Jones,⁶⁶ Drury and Jones.²⁶) Mosso, using a delicate balancing board, found that when a subject assumed the horizontal position after standing for some time, the weight of the feet end of the board only slowly decreased, in spite of the fact that presumably the excess blood leaves the lower extremities almost immediately.

Figs. 2 and 3 show the brass chambers used to determine the leg and arm volumes, respectively. Each chamber is used in an identical manner. Several water outlets tap the chamber, and a manometer on the outside indicates the water volume at any level. For a determination, the extremity is dipped into the chamber until it touches the bottom. An adjustable step in the leg chamber facilitates its use for individuals with shorter legs. With the extremity in place, water is run in until it overflows the desired outlet, the outlets below being clamped. The extremity is then removed and the volume difference is noted on the manometer, indicating the volume of the extremity.

Determinations were made of the difference in volume of the lower extremities of fourteen volunteer interns upon arising in the morning and retiring at night. The volumes were determined immediately upon arising and just before retiring.

In six cases of inflammation of the extremities, the decrease in tissue tension was compared with the decrease in volume after elevation.

In seventeen cases of inflammation of an extremity, the increased volume of the affected member over that of the opposite normal extremity was determined, except in a few cases where an estimation of the volume was made by measuring the circumference.

needle inserted into the tissues. The apparatus we used for direct measurement is shown in Fig. 1, and consists of a needle assembly which is connected to a pressure bulb manometer. A little saline solution is aspirated to any convenient level in the glass adapter which has a capillary bore. The needle is then inserted into the tissue to be studied and the needle assembly connected to the bulb and manometer by means of the cock. Pressure is then made on the rubber bulb, using the screw clamp, until the saline meniscus in the capillary just starts to descend. The manometer is then read, corrected for capillarity (about 2 to 3 cm. of saline solution for a 0.5 mm. capillary bore) and the reading assumed to be the tissue tension, really the resistance to distention.

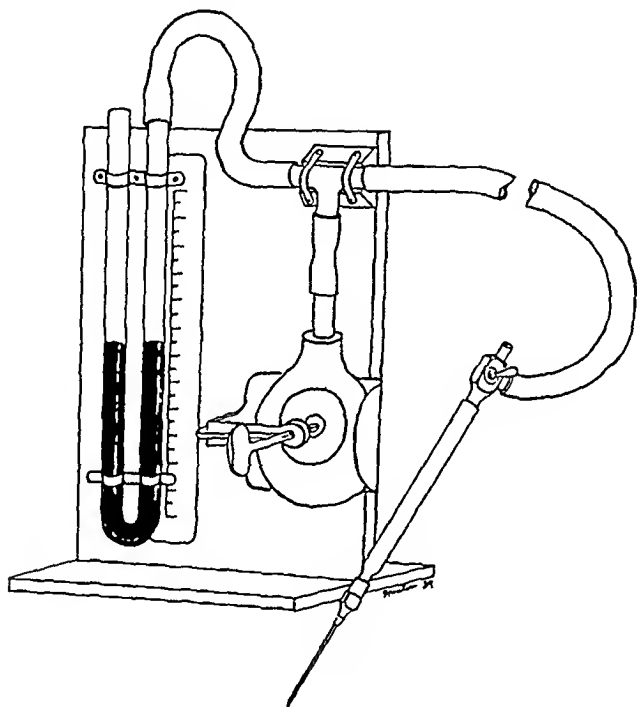


Fig. 1.—Apparatus for direct determination of tissue tension.

In a series of 103 patients visiting the medical outpatient clinic, the subcutaneous tissue tensions in the dorsum of the hand and mid thigh were determined.

Since it is known that the intramuscular pressure is higher in contracted than in relaxed muscle, we measured the intramuscular pressures in twenty-eight ambulatory patients and twenty-six patients who had had several days of bed rest. The muscles used were the biceps brachii, deltoid, quadriceps femoris, and the tibialis anticus.

Tissue Tensions in Inflammation.—In a series of fractures, the intramuscular and subcutaneous pressures were determined. In twenty-six

cases the pressures were determined before immobilization, and in 22 cases the intramuscular pressures were determined after partial immobilization. The pressures were also obtained in a shorter series of miscellaneous affections.

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Skin Surface Temperatures in Inflammation

In thirty-five cases of inflammation of the extremities, the skin surface temperatures of the normal and affected extremity in each case were determined. In many cases, volumes of the extremities and tissue tensions were also determined.

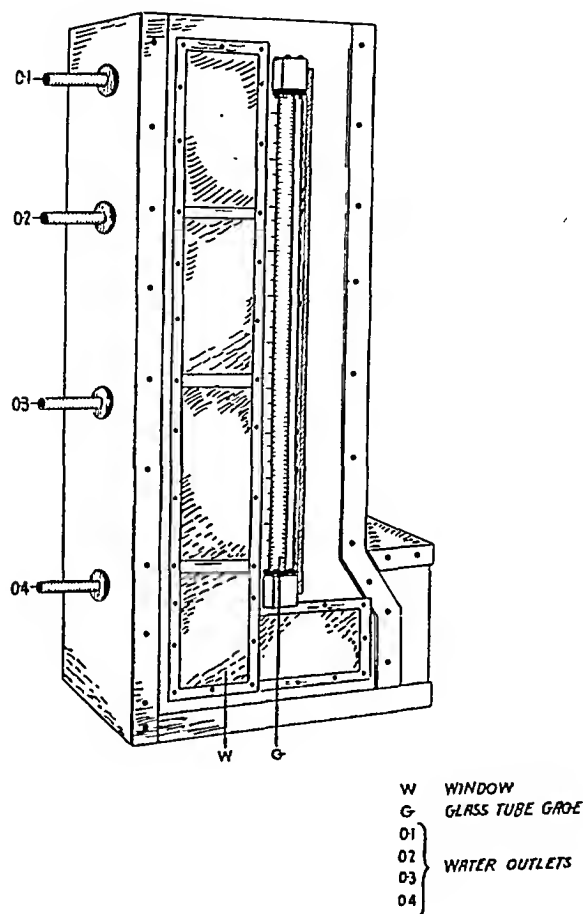


Fig. 2.—Brass chamber for measuring volume of lower extremity.

Protein Content of Serous Exudate in Human Inflammations

In ten cases of inflammations of the extremities, the specific gravity of the subcutaneous edema fluid was determined (Bellis⁸), and the protein content calculated as serum.

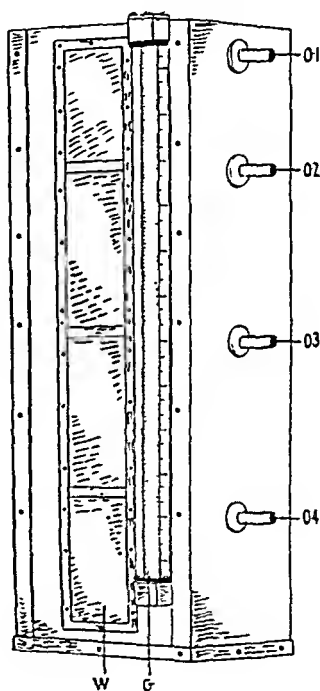
Inflammation in the Experimental Animal

For the purpose of experimentally induced inflammation, rabbits were used in most cases, the animal being anesthetized and one ear or extremity held in water at 60° C. for thirty seconds. In twelve hours this

gives an edematous extremity with most of the characteristics of human inflammation.

In five animals the affected extremity was placed in an air plethysmograph and the volume changes noted. In addition, the blister fluid was analyzed for protein and nonprotein nitrogen.

In four animals the edema fluid protein was compared with the plasma protein, the edema fluid pressure was determined, and the volumes of the extremities measured. Edema fluid was readily obtained, either by aspirating a blister or nicking the skin superficially and allowing it to flow out into a small test tube. Oxalate must be present to prevent coagulation, since the edema fluid contains so much protein that coagulation takes place quite readily.



W WINDOW
G GLASS TUBE GAGE
01 }
02 } WATER OUTLETS
03 }
04 }

FIG. 3.—Brass chamber for measuring volume of upper extremity.

To determine the efficiency of other irritants in producing inflammation, four piebald rats were injected subcutaneously with 0.1 c.c. of croton oil, 0.1 c.c. saturated sodium chloride solution, 0.1 c.c. half-saturated peptone solution, and 0.1 c.c. of mustard oil. Since equally

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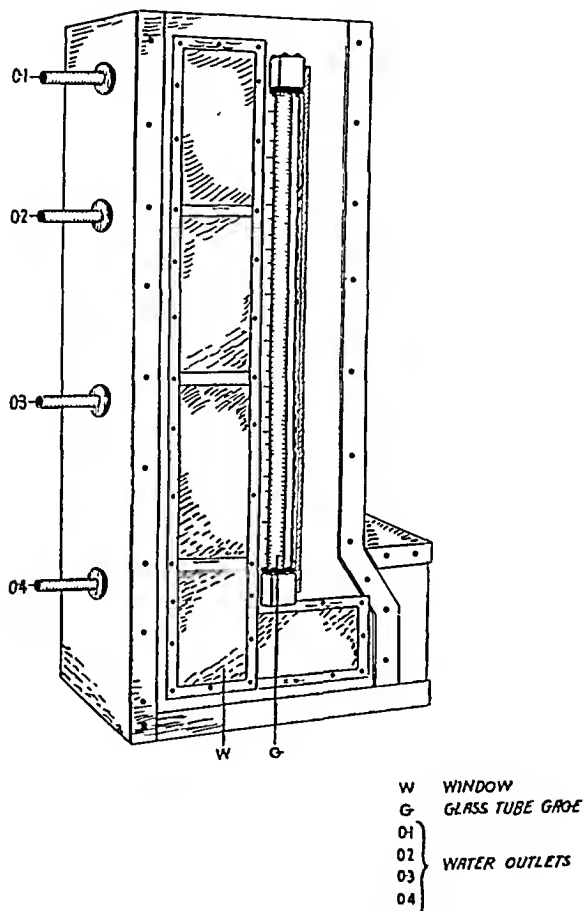


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in physiologic saline solution, adjusted to pH 7.3 with potassium acid phosphate solution communicating with a finely adjusted syringe, a mercury U manometer and the cannulating unit. The latter consists of fine flexible copper wire tubing attached by a rubber pressure tubing connector to a short length of heavy glass capillary tubing fixed in the jaws of the micromanipulator. In turn, by means of beeswax the heavy capillary tubing is fixed, end on, to the micropipette.

Although an electric heating apparatus is available for drawing the pipettes by a falling weight, better yields are obtained by drawing them by hand; that is, about one of every fifty meets the requirements. The diameter of the tip, examined under the microscope, should be between 8 and 15 μ in diameter and should be angled at 20 to 30°. A Spencer binocular dissecting microscope (magnification $\times 85$; 12.5 ocular; objective $\times 6.8$) in conjunction with a Spencer universal microscope lamp is

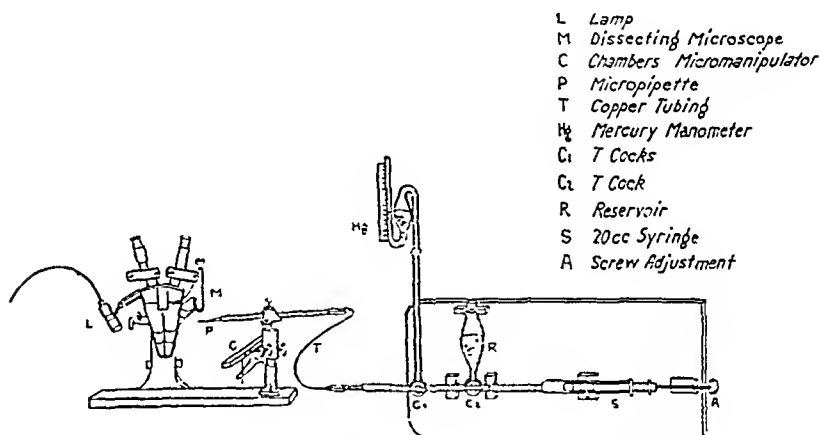


Fig. 4.—Apparatus for direct measurement of capillary pressure.

used. The pipette must be dust free, or else the fine tip will be plugged with dust granules. Therefore, a considerable quantity of citrate solution is used to flush the tip, the flushing process being observed through the microscope. The skin to be penetrated is steadied by sandbags and covered with a thin film of glycerin to avoid multiple reflections, and the microscope lamp is so angled that the reflection is not passed to the observer.

Using the Chambers micromanipulator, the pipette is passed through the skin, maintaining about 2 mm. Hg positive pressure. Immediately, the capillary seen a moment before as a curling string of corpuscles with a steady flow at one end and a pulsatile flow at the other end, disappears from view. This is due to a clamping shut of the little vessels, probably reflex. The observer then waits for three or four minutes, following which the capillary reopens. The pipette is then brought closer and

edematous areas were produced by each agent, some experiments were undertaken in rabbits. In one rabbit, 0.1 c.c. saturated sodium chloride solution and in another rabbit 0.1 c.c. half-saturated peptone solution was injected subcutaneously with no inflammation at the end of twenty-four hours sufficient for experiment.

Since croton oil seemed to have the desired inflammatory effect, inflammation was produced by this medium in three rabbits, the volumes of the inflamed ears and legs were determined, the edema fluid pressures determined, and the edema fluid protein compared with the plasma protein.

In four rabbits, complete physical studies were made. In each, the tarsosural region was depilated with barium sulfide and a sample of cardiac blood aspirated for control serum protein determination. The animal was then anesthetized and the depilated extremity immersed in water at 60° C. for one minute. Twenty-four hours later the serum protein was again determined and the animal reanesthetized. The tissue fluid pressure, its pH by the indicator method, and its protein content were determined. The pH of the blood plasma was similarly determined. Capillary pressures were obtained by intubation of capillaries in the inflammatory field. Finally, the volumes of the extremities were determined. The pH values were obtained because some investigators have cited significant changes in inflammation.

Any study of inflammation must, of necessity, consider the vacillating capillary pressure, the determination of which is delicate work. Capillaries in the living individual have been adequately described by many observers, but the determination of their intraluminal pressures has defied investigators until quite recently.

The blanching pressure and the pressure required to stop bleeding are inaccurate methods since they occasionally give values lower than venous pressure in the same individual. The figures so obtained are probably the pressures required to empty the subpapillary venous plexuses. The pressure necessary to prevent wheal formation also gives an abnormal reading. The slightest variations in the surroundings may lead to remarkable changes in the capillary diameter and its pressure; in fact, capillary pressures ranging from 1.5 to 71 mm. Hg have been recorded for the normal (Strax and deGraff⁵⁰).

Using the method of Lombard⁴¹ and Landis,³⁹ micropipettes can be drawn from fine glass tubes, and capillary cannulation accomplished with the Chambers¹⁸ micromanipulator. The apparatus* is diagrammed in Fig. 4 as assembled for use. Essentially, it is composed of two units functioning independently or dependently. On the right is the pressure system. This consists of a reservoir of 0.3 per cent sodium citrate

*Loaned through the courtesy of Dr. George L. Fahr of the Minneapolis General Hospital.

directed toward the mid-portion of the capillary, and, if possible, opposite to the direction of the stream. Entrance into the vessel is evident when a stream of corpuscles travels up the pipette. Gradual pressure is then made by means of the syringe until the corpuscles pulsate but do not move. The pressure is then read on the mercury manometer.

Capillary intubation in the anesthetized rabbit is especially difficult. The rapid, jerky respirations not only make it difficult to focus the capillary but tax the patience of the operator in his efforts to pierce the jerking vessel. In fact, penetration must be accomplished in an interval between respirations. Fracturing of the cannula tip, making its discard necessary, is often a discouraging result of the respiratory jerking of the leg.

The animals were anesthetized with intravenous pentobarbital sodium, and no information is available as to the effect of the anesthetic itself on the capillary pressure.

In order to study the flow in the lymphatics from inflamed areas, three dogs were used. Each animal was anesthetized with intraperitoneal pentobarbital sodium (35 mg. per kilogram). In one, the skin of the front of the foreleg and back of the hindleg was incised and retracted and 2 c.c. of 2 per cent aqueous trypan blue injected into each foot pad. Light passive motion of the foot immediately brought the lymphatics into view as blue streams of a more purple color than the veins. Using a hand lens, a large lymphatic trunk was cannulated with a fine glass cannula. With an assistant counting the number of drops falling, the flow was determined after massage and passive motion, and, finally, after immersing the paw in a beaker of water at 60° C. for one minute. An identical procedure was done in a second animal except that the heating temperature was 45° C. In the third dog, lymph flow was determined without heating the paw.

RESULTS

Position and Blood Flow in the Patient

Arterial Blood Pressure.—The average radial systolic blood pressure in twelve individuals was 27 mm. Hg higher with the extremity in the horizontal position than in the elevated position, and 44 mm. Hg higher with the extremity dependent than in the elevated position. An average increase of 17 mm. Hg took place when the extremity was brought from the horizontal to the dependent position (Table I).

Skin Surface Temperatures.—In five normal individuals, the average skin surface temperature of the finger tip was 4.4° C. lower than at horizontal position after elevating the extremity perpendicular to the horizontal trunk for an hour (Table II).

In six individuals, the temperatures in the foot and toes were depressed from 2 to 5° after elevation at 60° with the horizontal position for twelve hours (Table III is a typical case).

TABLE I
EFFECT ON SYSTOLIC BLOOD PRESSURE
(MM. HG) OF POSITIONING ARM

NO.	HORIZONTAL (H)	ELEVATED (E)	DEPENDENT (D)	DIFFERENCES		
				I-H	H-D	E-D
1	96	80	130	16	34	50
2	106	90	120	16	20	36
3	120	92	132	28	12	40
4	106	94	116	12	10	22
5	108	90	114	18	6	24
6	120	98	132	22	12	34
7	110	76	116	34	6	40
8	88	68	110	20	22	42
9	108	66	116	42	8	50
10	124	80	150	44	26	70
11	120	76	148	44	28	72
12	110	76	128	34	18	52
Average				27	17	44

TABLE II
EFFECT OF ELEVATION ON SKIN SURFACE
TEMPERATURES OF FINGERS (° C.)

NO.	HORIZONTAL	ELEVATED	TEMPERATURE DIFFERENCE
1	29.3	25.5	3.8
2	30.0	26.0	4.0
3	27.4	24.0	3.4
4	30.4	24.2	6.2
5	32.5	27.6	4.9
Average			4.4

TABLE III
SKIN SURFACE TEMPERATURES (° C.) BEFORE AND AFTER ELEVATION
OF RIGHT LOWER EXTREMITY FOR TWELVE HOURS

REGION	BEFORE ELEVATING THE RIGHT LEG		AFTER ELEVATING THE RIGHT LEG	
	RIGHT	LEFT	RIGHT	LEFT
Upper thigh	33.7	33.7	32.5	32.3
Lower thigh	33.1	32.9	32.3	32.5
Upper tibia	33.5	33.1	29.3	32.1
Ankle	34.5	34.3	29.3	33.1
Dorsum foot	33.7	33.7	27.1	33.7

TABLE IV
EFFECT OF TWELVE HOURS' SEMI-FOWLER'S POSITION ON SKIN SURFACE
TEMPERATURES OF LOWER EXTREMITIES (° C.)

REGION	BEFORE	AFTER
Upper thigh	32.0	32.2
Lower thigh	31.0	32.0
Upper tibia	29.8	31.0
Middle tibia	31.0	31.6
Ankle	29.6	30.4
Dorsum foot	27.4	29.2
Base great toe	26.0	29.4
Medial great toe	22.2	23.4

Increase in volume = 350 c.c.

TABLE VII
TENSILE TENSIONS BEFORE AND AFTER IMMOBILIZATION OF FRACTURES (TENSIONS IN MM. Hg.)

ART. FRACTURES	BEFORE FAVORIZATION				AFTER PARTIAL IMMOBILIZATION			
	AV., INJURED SIDE	RANGE	AV., UNIN- JURED SIDE	RANGE	NUMBER OF CASES	AV., INJURED SIDE	RANGE	NUMBER OF CASES
1. Humerus								
a. intramuscular	15-16	6-28	5	0-12	7	5-6	2-12	3
b. subcutaneous	13	3-36	1-2	0-4	6	0-1	0-3	5
2. Forearm								
a. subcutaneous	16	16-16	6	4-8	2	2	0-1	2
3. Shaft femur								
a. intramuscular	14	14	6	6	1	2	2	1
4. Knee								
a. intramuscular	20	20	6	20	1	---	---	---
b. subcutaneous	16	10-22	5	0-10	2	---	---	---
5. Leg								
a. intramuscular	18	12-26	8-9	8-10	3	---	---	---
b. subcutaneous	15	6-24	0	0-0	2	6	0-12	2
6. Ankle								
a. subcutaneous	10	10	0	0	1	---	---	---
7. Clavicle								
a. subcutaneous	8	8	0	0	1	---	---	---
FRACTURES AFTER PARTIAL IMMOBILIZATION								
1. Humerus								
a. Forearm	---	---	---	---	---	4	4	1
b. Femur	---	---	---	---	---	2	2	1
4. Knee	---	---	---	---	---	1-2	0-4	4
5. Leg	---	---	---	---	---	0	0-0	2
	---	---	---	---	---	0	0	1

After twelve hours in the semi-Fowler's position, the skin surface temperatures of the lower extremity were found to increase as much as 3.4° C. and the volume of the extremity to increase 350 c.c. Control readings were previously obtained in the horizontal position (Table IV).

Tissue Tensions in the Patient

Normal Tissue Tension.—In 103 routine outpatients, the subcutaneous tissue tension on the dorsum of the hand averaged 1.8 mm. Hg (mean 2.2 mm. Hg), and the tension on the dorsum of the thigh averaged 2.5 mm. Hg (mean 2.7 mm. Hg) (Table V).

TABLE V
NORMAL SUBCUTANEOUS PRESSURES (RESISTANCE TO DISTENTION)
IN 103 AMBULANT PATIENTS (MM. Hg)

DORSUM HAND		MID-THIGH	
NUMBER OF PATIENTS	PRESSURE	NUMBER OF PATIENTS	PRESSURE
11	0	3	0
42	1	20	1
23	2	34	2
13	3	22	3
8	4	18	4
5	5	6	5
1	6		
Average	1.8		2.5
Mean	2.2		2.7

In twenty-eight ambulatory patients, the intramuscular tension at rest averaged 3 to 7 mm. Hg higher than in twenty-six patients undergoing bed rest (Table VI).

TABLE VI
NORMAL INTRAMUSCULAR PRESSURES (MM. Hg)

	NO. CASES	REGION	AV. PR.	RANGE
Tensions in ambulatory patients	16	Deltoid	4.5	2.8
	10	Quadriceps femoris	3.4	1.6
	2	Tibialis anterior	7	6.8
Tensions after several days of bed rest	2	Biceps brachii	0	0
	14	Deltoid	0+	0.3
	10	Quadriceps femoris	0.1	0.4

Tissue Tension in Inflammation.—In acute fractures, the average tissue pressures ranged from 8 to 16 mm. Hg, compared with the average 0 to 9 mm. Hg for the uninjured side. After immobilization, the average tissue pressures on the injured side were 0 to 12 mm. Hg, compared with 0 to 14 mm. Hg for the uninjured side (Table VII).

In a series of miscellaneous inflammations, the subcutaneous tissue pressure averaged 4 to 20 mm. Hg, compared with 0 to 4 mm. Hg on the uninjured side. In five cases of cardiac decompensation the subcutaneous tissue pressures ranged from 13 to 22 mm. Hg (Table VIII).

In a series of twenty cases of inflammation of the extremity in which the skin surface temperatures were also determined, the tissue tensions on the affected sides were always higher than on the normal. In one case, a subcutaneous pressure of 56 mm. H₂O was observed (Table IX).

TABLE IX

MAXIMUM INCREASES IN SKIN SURFACE TEMPERATURE (° C.), TISSUE TENSION (CM. H₂O), VOLUME (C.C.), AND CIRCUMFERENCE (CM.) OF INFLAMED EXTREMITIES, ABOVE CORRESPONDING NORMAL EXTREMITY (35 CASES)

CASE NO.	MAXIMUM TEMPERATURE INCREASE	MAXIMUM TISSUE TENSION INCREASE	MAXIMUM VOLUME INCREASE	MAXIMUM CIRCUMFERENCE INCREASE
1	2.4	---	---	---
2	3.9	---	---	---
3	2.8	---	---	---
4	3.0	---	---	---
5	3.2	---	---	---
6	3.2	---	---	---
7	7.2	---	---	---
8	3.6	---	---	---
9	1.4	---	---	---
10	2.4	---	---	---
11	3.2	---	---	---
12	4.4	---	---	---
13	2.6	---	---	---
14	5.8	---	---	---
15	5.4	---	---	---
16	3.0	---	---	---
17	0.8	10.0	---	---
18	1.8	2.6	---	---
19	1.2	18.0	1000	---
20	1.4	7.0	200	---
21	0.6	10.0	1650	---
22	1.7	5.0	500	---
23	1.4	27.0	2900	---
24	2.0	44.0	4150	---
25	1.0	22.0	1150	---
26	0.8	24.0	1500	---
27	1.1	8.0	900	---
28	1.6	26.0	4500	---
29	1.2	13.0	851	---
30	3.1	11.0	800	---
31	1.1	10.0	---	6.5
32	3.8	13.0	---	9.0
33	0.6	12.0	---	5.0
34	2.0	1.0	---	5.0
35	0.6	1.0	---	7.0

Position and Volume Changes in the Human Being

In fourteen interns the increases in volume of the lower extremity at night over that in the morning ranged from 50 c.c. to 800 c.c. Expressed as increase per 100 c.c. of extremity, the increases ranged from 0.5 c.c. per 100 c.c. to 7.3 c.c. per 100 c.c. These increases amounted to 2 to 7 per cent of the leg volume (Table X).

In six cases of infection of the upper or lower extremity, the volume decreases after elevation ranged from 365 c.c. to 1,617 c.c. (Table XI).

TABLE VIII
TISSUE PRESSURES IN MISCELLANEOUS AFFECTIONS (MM. HG)

AFFECTION	BEFORE IMMOBILIZATION					AFTER IMMOBILIZATION				
	AV., INJURED SIDE	RANGE	AV., UNIN- JURED SIDE	RANGE	NUMBER OF CASES	AV., INJURED SIDE	RANGE	AV., UNIN- JURED SIDE	RANGE	NUMBER OF CASES
A. Arthrodeses of shoulder (all intramuscular)	---	---	---	---	---	6	4-8	17	16-18	2
B. Acute shoulder dislocations (subcutaneous)	4	4	0	0	1	---	---	---	---	---
C. Infections of extremities										
1. Skin elbow (subcutaneous)	20	20	3	3	1	---	---	---	---	---
2. Finger (subcutaneous)	16	16	4	4	1	---	---	---	---	---
3. Knee (quadriceps femoris)	---	---	---	---	---	0	0	4	4	1
1. Osteomyelitis leg (intramuscular)	---	---	---	---	---	0	0	5	5	1
D. Infection of buttock (subcutaneous)	12	---	0	---	1	---	---	---	---	---
E. Residual poliomyelitis (intramuscular)										
1. Deltoid	---	---	---	---	---	0	0-0	6	2-8	2
2. Quadriceps fem.	---	---	---	---	---	2	2	4	4	1
3. Tibialis anter.	---	---	---	---	---	0	0	4	4	1
F. Cardiac decompensation										
1. Tibialis anterior	21-22	14-30	(before medical treatment)		2	0	0	(after medical treatment)		1
a. Intramuscular	12-13	8-14			3					
b. Subcutaneous										
G. Hemangioid telangioma of shoulder girdle										
a. shoulder girdle	50	---	0	---						
b. pronator teres	30	---	4	---						
c. dor-sum hand	23	---	0	---						

TABLE XII

SPECIFIC GRAVITIES OF SUBCUTANEOUS EDEMA FLUIDS IN INFLAMMATIONS OF THE EXTREMITIES

CASE	SPECIFIC GRAVITY	PROTEIN (GM. PER 100 C.C.) AS SERUM
1	1.028	7.2
2	1.026	6.5
3	1.024	5.8
4	1.025	6.2
5	1.018	3.7
6	1.019	4.1
7	1.025	6.2
8	1.028	7.2
9	1.030	7.9
10	1.026	6.5

The blister fluid protein content ranged from 4.6 to 6.3 per cent and the nonprotein nitrogen content from 48 to 126 mg. per cent (Table XIII, a, b, c, d, and e).

In four other rabbits inflammations of the ear by heat caused volume increases ranging from 11 to 25 c.c. In the heat inflammations of the leg, the volume increases ranged from 109 to 60 c.c. The edema fluid protein levels ranged from 3.9 to 4.7 per cent, which were about equal to the plasma protein levels. The tissue pressures in the involved side ranged from 12 to 28 mm. Hg (Table XIII, f, g, h, and i).

TABLE XIII

EFFECT OF EXPERIMENTAL INFLAMMATION ON VOLUME CHANGE, PLASMA PROTEIN, TISSUE FLUID PROTEIN, AND TISSUE PRESSURE

	CASE	PLASMA PROTEIN (GM. PER 100 C.C.)		EDEMA FLUID		VOLUME INCREASE (C.C.)	TISSUE TENSION (MM. HG)	TIME INTERVAL (HOURS)
		PREOP- ERATIVE	POSTOP- ERATIVE	PRO- TEIN (GM. PER 100 C.C.)	N.P.N. (MG. PER 100 C.C.)			
Heat Inflam- mation	a (Ear)	--	--	--	--	9.5	--	2.5
	b	--	--	5.2	15.2	12.5	--	6
				5.1				
	c	--	--	4.6	70.6	5	--	2
	d	--	--	6.3	126	6	--	4
	e	--	--	5.2	79	17	--	11
				5.8	81			
	f	--	1.6	4.6	--	60	28	8
				4.7				
	g	1.9	4.1	3.9	--	35	22	6
Croton Oil In- flammation		4.7	1.7	1.1	--	25 (Ear)		
	h	4.5	3.2	1.1	--	10	18	21
			3.5	1.5				
	i	5.1	5.2	4.1	--	25	12	36
						11 (Ear)		
	j	--	2.5	3.2	--	--	28	21
	k	1.6	2.6	3.3	--	15	16	21
				3.5		15 (Ear)		
	l	6.3	5.0	1.6	--	--	28	21
		6.2	5.3	4.7				

In infections of the lower extremity, as great an increase in volume as 4,500 c.c. was observed over that in the corresponding normal extremity (Table IX).

Skin Surface Temperatures in Human Inflammation

In thirty-five cases of inflammations of the upper or lower extremities, there were increases of skin temperature up to 7° C. on the affected side (Table IX).

TABLE X

DIFFERENCE IN VOLUME OF ONE LOWER EXTREMITY IN 14 HEALTHY YOUNG MEN
BETWEEN ARISING IN MORNING AND RETIRING AT NIGHT

CASE	INITIAL LEG VOLUME	INCREASE (C.C.)	INCREASE PER 100 C.C. OF EXTREMITY
1	9250	50	0.5
2	10250	600	6.0
3	9000	300	3.3
4	11150	550	5.0
5	11250	100	1.0
6	9950	500	5.0
7	13050	650	5.0
8	10900	800	7.3
9	8650	200	2.3
10	10150	300	2.0
11	9750	250	2.5
12	10200	500	5.0
13	11550	550	5.0
14	10750	350	3.0

TABLE XI

TISSUE TENSION AND VOLUME CHANGES OF INFLAMED EXTREMITIES ATTENDING
ELEVATION

CASE	AREA INVOLVED	TISSUE TENSION (MM. Hg)		VOLUME DECREASE (C.C.)	TIME INTERVAL
		1	2		
1	Furuncle, elbow	12	4	447	15 days
2	Thrombophlebitis, leg	20	8	870	12 hours
3	Thrombophlebitis, leg	40	4	365	14 days
4	Phlebitis, arm	--	--	415	4 hours
5	Thrombophlebitis, leg	10	2	988	4 days
6	Cellulitis, leg	--	--	1617	17 days

Protein Content of Serous Exudates in Human Inflammation

In ten cases of inflammation of the extremities, the specific gravity of the edema fluid was found to range from 1.019 to 1.030, corresponding to protein contents of 4.1 to 7.9 per cent, calculated as serum (Table XII).

Correlation of Physical Factors in Experimental Inflammation

Capillary Pressures, Tissue Tensions, Tissue Fluid Protein, Plasma Protein, pH of Tissue Fluid, Volume Changes.—In four rabbits and one cat, heat inflammation caused increases in volume ranging from 5 to 10 c.c. distal to the tarsosural joint, as measured in the air plethysmograph.

TABLE XII

SPECIFIC GRAVITIES OF SUBCUTANEOUS EDEMA FLUIDS IN INFLAMMATIONS OF THE EXTREMITIES

CASE	SPECIFIC GRAVITY	PROTEIN (GM. PER 100 C.C.) AS SERUM
1	1.028	7.2
2	1.026	6.5
3	1.024	5.8
4	1.025	6.2
5	1.018	3.7
6	1.019	4.1
7	1.025	6.2
8	1.028	7.2
9	1.030	7.9
10	1.026	6.5

The blister fluid protein content ranged from 4.6 to 6.3 per cent and the nonprotein nitrogen content from 48 to 126 mg. per cent (Table XIII, a, b, e, d. and e).

In four other rabbits inflammations of the ear by heat caused volume increases ranging from 11 to 25 c.e. In the heat inflammations of the leg, the volume increases ranged from 109 to 60 c.e. The edema fluid protein levels ranged from 3.9 to 4.7 per cent, which were about equal to the plasma protein levels. The tissue pressures in the involved side ranged from 12 to 28 mm. Hg (Table XIII, f, g, h, and i).

TABLE XIII

EFFECT OF EXPERIMENTAL INFLAMMATION ON VOLUME CHANGE, PLASMA PROTEIN, TISSUE FLUID PROTEIN, AND TISSUE PRESSURE

	CASE	PLASMA PROTEIN (GM. PER 100 C.C.)		EDEMA FLUID		VOLUME INCREASE (C.C.)	TISSUE TENSION (MM. HG)	TIME INTERVAL (HOURS)
		PREOP- ERATIVE	POSTOP- ERATIVE	PRO- TEIN (GM. PER 100 C.C.)	N.P.N. (MG. PER 100 C.C.)			
				100 C.C.)	100 C.C.)			
Heat Inflammation	a (Cat)	--	--	--	--	9.5	--	2.5
	b	--	--	5.2	48.2	12.5	--	6
				5.4				
	c	--	--	4.6	70.6	5	--	2
	d	--	--	6.3	126	6	--	4
	e	--	--	5.2	79	17	--	11
				5.8	84			
	f	--	1.6	4.6	--	60	28	8
				4.7				
	g	1.9	1.1	3.9	--	35	22	6
Croton Oil Inflammation		4.7	1.7	4.1	--	25 (Ear)		
	h	4.5	3.3	1.4	--	10	18	21
			3.5	1.5				
	i	5.4	5.2	1.1	--	25	12	36
						11 (Ear)		
Croton Oil Inflammation	j	--	2.5	2.2	--	--	28	21
	k	1.6	3.6	3.3	--	15	16	21
				3.5		15 (Ear)		
	l	6.7	5.9	4.6	--	--	28	21
		6.2	5.3	4.7				

In three rabbits with ear and leg inflammations by croton oil, the ear volume in one increased 15 c.c. and the leg volume 45 c.c. The edema fluid proteins at the same time ranged from 2.2 to 4.7 per cent and the plasma proteins from 2.5 to 5.3 per cent (Table XIII, j, k, and l). Pre-operative plasma protein levels ranged from 4.5 to 6.3 per cent. In two rabbits the tissue tensions in the inflamed area were 28 and 16 mm. Hg, respectively. Control tissue tensions in this series were 0 to 2 mm. Hg.

In four rabbits in which heat inflammation of the leg was produced, the serum protein was found to be lowered and the edema fluid protein levels ranged from 2.8 to 4.1 per cent. Capillary pressures ranged from 31 to 40 mm. Hg in the inflamed area, while the extremities increased in volume, ranging from 10 to 65 c.c. In three of these animals, simultaneous determinations of plasma and edema fluid pH showed no practical differences (Table XIV).

TABLE XIV

EFFECT OF EXPERIMENTAL HEAT INFLAMMATION IN RABBIT EXTREMITY ON FACTORS WHICH REGULATE FLUID INTERCHANGE

CASE	PLASMA PROTEIN (GM. PER 100 C.C.)		EDEMA FLUID (GM. PER 100 C.C.)		TISSUE TENSION (MM. HG)	CAPILLARY PRESSURE (MM. HG)	VOLUME INCREASE (C.C.)
	PRE- OPERATIVE	POST- OPERATIVE	PROTEIN	PH			
a	6.4	6.0	4.1	--	31	40	24
b	4.5	3.8 (pH 7.6)	2.8	7.4	20 (Control = 0)	31	10
c	4.6	4.3 (pH 7.5)	3.1	7.4	16 (Control = 0)	33	55
d	4.0	3.5 (pH 7.5)	3.1	7.5	26 (Control = 4)	27	65

Lymph Flow.—The lymph flow through the cannulated lymphatic of the dog's leg is practically zero at rest, but is increased by massage or passive motion. In one of the three animals studied, heating the extremity to 45° C. caused the lymph to flow out of the cannula in a steady stream (Table XV).

TABLE XV

EFFECT OF HEAT INFLAMMATION ON LYMPH FLOW IN EXTREMITY OF DOG

NO.	FLOW DURING INACTIVITY	VOLUME FLOW AFTER MASSAGE OR MOTION	TISSUE TENSION (MM. HG)
1	0 in 3 min.	(a) 3 c.c. in 3 min. (b) 0 in 2 min. after heating at 60° C.	-- --
2*	0 in 2 min.	.25 c.c. in 1 min. (clotting of lymph in cannula)	11
3	0 in 3 min.	(a) 2.0 c.c. in 3 min. (b) 4 to 5 c.c. per min. after heating to 45° C.	-- --

*Twenty-four hours after inflammation.

CLINICAL APPLICATIONS

Infections of the Extremities

Types of Casts.—Hilton³⁶ wrote a fascinating and informative treatise on rest and pain in which he stressed the importance of rest in the treatment of infections. Those skilled in the treatment of tuberculosis will attest to this fact. A short time later Dennis²⁴ pointed out the great value of immobilization in plaster in the treatment of compound fractures, and Orr⁴⁸ adopted rigid immobilization in plaster as a constant sequel to sequestrectomy for chronic osteomyelitis, shortly thereafter employing closed plaster casts and massive vaseline packs together with extensive osteotomy in acute osteomyelitis.

In the surgical clinic of the University of Minnesota Hospitals, the essential treatment of acute infections of the extremities has been (a) rest by immobilization of the entire extremity involved in a plaster cast including the trunk, and (b) elevation by positioning the affected member in the cast in such a manner as to most rapidly drain the edema fluid toward the heart by gravity. Fig. 5 shows the type of shoulder splica applied in the event of infection involving the upper extremity. With the arm in mid-elevation the extremity is above heart level when the patient is standing, sitting, or lying.

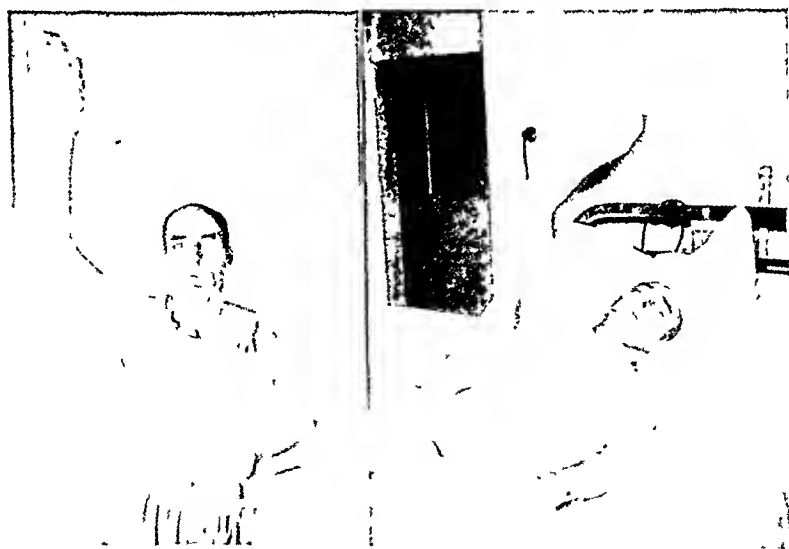


Fig. 5—Type of shoulder splica applied for inflammation of upper extremity

Appropriate windows are cut in the cast to permit frequent observation of the infected area; when there is definite evidence of suppuration, not before, a small incision is made for evacuation of the exudate through the cast window. Large incisions have no additional advantage, producing only more trauma to tax the patient's already burdened healing powers.

In acute osteomyelitis of the tibia, for example, a body plaster is applied extending from the waist to the toes on the affected side, the affected member being placed in elevation (Fig. 6). A window is cut in the plaster directly over the tender area permitting incision when evidence of abscess formation is present. The only type of case in which early incision is warranted is acute tenosynovitis. In such cases, the necessity of early opening of the tendon sheath to preserve the nutrition and identity of the tendon has been pointed out by Kanavel.³⁷

The immobilization which can be secured by a body cast is ever so much more efficient than that obtained by any other method. Sandbags, traction, voluntary rest, and other measures do not begin to afford the relaxation and rest to an inflamed extremity that an adequate plaster cast will. A patient with an infected knee joint, treated with adequate traction, may cry with pain when the bed is touched. After the application of a cast the patient can be turned over in bed without causing him the slightest discomfort.



FIG. 6—Type of hip splier cast applied for inflammation of the lower extremity

Results of Immobilization and Elevation—A questionnaire was mailed to all patients hospitalized in the University of Minnesota Hospitals in the six-year period from January, 1931, to December, 1939, for infections of extremities and who were treated by immobilization in plaster

casts. In the letter, the patient was asked to describe his present condition or to return to the outpatient clinic for examination. The total number of cases finally available for tabulation was 116 (Table XVIa). Forty-one, or 35.3 per cent, returned for examination; forty-nine, or 42.2 per cent, replied by mail; eighty-three, or 19.8 per cent, did not reply but were recently examined in the outpatient clinic; and three, or 2.5 per cent, were dead.

TABLE XVI

CLASSIFICATION OF 116 PATIENTS TREATED BY IMMOBILIZATION IN PLASTER CASTS
FOR INFLAMMATION OF THE EXTREMITIES

	NO.	PER CENT
a. Results of mailing questionnaires:		
Patients returning for examination	41	35.3
Additional replies	49	42.2
Those not replying but recently examined	23	19.8
Deaths	3	2.5
Total number of patients in study	116	100.0
b. Classification of inflammations included in this study:		
Hand and forearm	25	21.5
Lower extremity	8	6.9
Osteomyelitis:		
acute	12	10.3
chronic	56	48.3
Primary septic arthritis	15	13.0
Total	116	100.0

It was found (Table XVIb) that twenty-five cases, or 21.5 per cent, were infections of the hand or forearm; eight, or 6.9 per cent, were lower extremity infections, twelve, or 10.3 per cent, were acute osteomyelitis; fifty-six, or 48.3 per cent, were chronic osteomyelitis; and fifteen, or 13.0 per cent, were primary septic arthritis.

Good results, that is rapid control of the infection with healing, were obtained in 72.2 per cent; fair results, that is control of the infection with delay or recurrence, were obtained in 21.6 per cent; poor results, that is uncontrolled infections, were obtained in 6.0 per cent. These results are itemized in Table XVII. Itemization of the patients in each pathologic classification is recorded in Table XVIII.

TABLE XVII

SUMMARIZED RESULTS OF TREATMENT OF INFLAMMATIONS OF EXTREMITIES BY
IMMOBILIZATION AND ELEVATION IN PLASTER CASTS

TYPE OF INFECTION	GOOD (RAPID CONTROL WITH HEALING)		FAIR (CONTROL WITH DELAY OR RECURRENT)		POOR (INFECTION NOT CONTROLLED)	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Hand and forearm	20	80	5	12.0	2	8
Lower extremity	7	87.5	1	12.5	0	0
Septic arthritis	10	66.6	4	26.6	1	6.6
Osteomyelitis:						
acute	8	66.6	3	25.0	1	8.3
chronic	34	60.7	18	21.1	4	7.2
Totals	79	72.2	29	21.6	8	6.0

TABLE XVIII

DETAILED RESULTS IN TREATMENT OF INFECTIONS BY IMMOBILIZATION IN PLASTER

	TYPE	NO.	TREATMENT	DAYS IN CAST (AV.)	DAYS IN HOS- PITAL (AV.)	RESULT
Hand and forearm in- fections	Traumatic	8	Shoulder spica	26	20	3 Good 3 Ankylosis 2 Finger ampu- tated
	Fascial space	6	Shoulder spica	11	15	3 Excellent 2 Stiff or anky- losed 1 Amputation of digit advised
	Lymphadenitis	1	Shoulder spica	6	14	1 Excellent
	Tenosynovitis	1	Shoulder spica	20	40	Ankylosis
	Soft tissue in- fection with bone involve- ment	4	Shoulder spica	25	50	3 Healed with ankylosis
	Furuncle	1	Arm cast, suspended	5	7	1 Amputation through carpus Death; septic- emia and lung abscess
	Forearm	4	Shoulder spica	10	16	3 Excellent 1 Stiff elbow
Lower ex- tremity in- fections	Cellulitis	4	Hip spica, long leg	12	14	3 Good 1 Ankylosis
	Gunshot	1	Hip spica	180	135	Draining; crutches Excellent
	Puncture (manure fork)	1	Hip spica	25	40	Excellent
	Infected vari- cose ulcer	1	Long leg	30	35	Good
Primary septic arthritis	Multiple	2	Spica	92	240	Ankylosis or limitation
	Sacroiliac and hip	3	Hip spica	80	68	Ankylosis in all
	Knee	6	Hip spica or long leg	39	25	4 Ankylosis 2 Good function; both children aged 2 yrs.
	Ankle	2	Long leg Short leg	13 2 yrs.	14	1 Excellent 1 Ankylosis; good function
	Elbow	1	Arm cast suspended	10	48	Ankylosis
	Hip, traumatic	1	Spica	5	7	Death
Acute osteo- myelitis	Tibia or fibula	4	Hip spica; long and short leg casts	84	51	Good in all
	Femur	3	Hip spica	57	45	2 Good 1 Death; pneumo- nia
	Radius or ulna	2	Shoulder spica; arm suspended	26	11	1 Good 1 Ankylosis of el- bow
	Sacroiliac Scapula	2 1	Body cast Airplane	62 --	22 10	Good Good
Chronic osteomye- litis	56 cases; aver- age duration 8.4 yrs. when first seen		Casts	190	83	34 Good (16 ob- served more than 2 yrs.) 18 Recurrences 4 Amputations 2 Fair 18 Ankylosis

DISCUSSION

Effect of Immobilization

Although it has been suggested that immobilization causes atrophy, the actual evidence of any great degree of atrophy is lacking. The work of Sherrington and others has adequately demonstrated the proprioceptive nature of muscle tone, a phenomenon which can be initiated by such actions as passive changes in the position of the head. Some experimenters have observed minimal atrophy in the extremities of animals encased in plaster casts, but they offer evidence that such minimal atrophy is temporary and may be almost obviated by properly applied casts. It cannot be proved that normal muscles, immobilized in casts, are in a state of inactivity; rather, muscle tone is preserved and normal voluntary motion, although partly isometric, begins with the disappearance of pain.

Inflammation and Pain.—Inflammation is in large part a reflex act initiated by pain (Odermatt,⁴⁶ Rosenbach,⁵³ Ricker and Regendanz⁵²). Spiess⁵⁵ emphasized that anesthetized wounds undergo less inflammation, and he stated that there is a direct relationship between anesthesia and healing. He noted that the more painful a wound is the more it becomes inflamed. If the pain is removed by means of a local anesthetic, the inflammation diminishes to an extraordinary degree.

Bruee¹⁴ showed experimentally that conjunctival anesthetics prevented inflammation, that the initial vasodilation in inflammation was an axon reflex, and that the development of edema is dependent upon the intactness of the axon reflex. In his experiments he used alypin, a local anesthetic, to prevent mustard oil inflammation in the eye. Bardy⁶ advocated the use of morphine to reduce inflammation and stated that *dolor* was responsible for *turgor*, *rubor*, and *calor*.

Inflammation and Rest.—Since the lymphatic channels through which infections spread lie in the fascias overlying the muscles, lessening of muscle movement which accompanies immobilization in plaster serves to minimize dissipation of the infection, and must be an important factor in aiding the natural defenses of the body in localizing the infection. Experimentally, Beecher⁷ has demonstrated the marked lymph flow attending muscular activity.

Adler,³ speaking of tissue fluid, wrote, "The fluid spreads with more or less ease from one lymph space to another, the propelling forces being diffusion and mechanical pressure. The latter is caused, first, by contracting the muscles surrounding the lymph spaces, and second, by gravity and external mechanical pressure (massage)." The excellent work of McMaster, Hudeak, and Parsons⁴³ illustrates the readiness with which the gentlest massage increases lymph flow.

Effect of Elevation

Elevation of an inflamed part diminishes the edema and increased venous pressure and reduces the temperature of the inflamed part. Because of the abnormal permeability, edema can be only diminished, since the capillary wall is then much more permeable to protein which escapes into the tissue spaces. Owing to the diminished transudation of fluid it effects, and the introduction of the effect of gravity on blood flow and on the edema fluid forming and already formed, elevation definitely reduces the tissue tension and volume of the extremity. Friedrich³¹ taught that the rising tissue pressure compressed capillaries and caused gangrene.

Thus, the Fowler's position would be indicated for infections of the head and neck, and the Trendelenburg position in pararectal, scrotal, pelvic, and lower abdominal inflammations. Carrier and Rehberg¹⁷ and Turner⁶¹ showed that when the hand is above the base of the heart, capillary pressure is low, and when dropped below, the increase of capillary pressure is almost identical with the theoretic increment due to the hydrostatic pressure of the column of the venous blood.

Relation Between Capillary Pressure, Plasma Oncotic Pressure, Tissue Tension, and Tissue Oncotic Pressure.—Graham,³³ who first used the term colloid, mentioned that plasma colloids might exert an osmotic pressure in the blood. After Starling's demonstration⁵⁷ of the colloid osmotic pressure exerted by the plasma proteins, Schade and his co-workers⁵⁵ showed that in inflammation, especially in suppuration, the osmotic pressure of the tissue fluid may be as high as eleven atmospheres, and, therefore, inflammatory edema was merely an entire osmotic phenomenon. He gave proper importance, however, to the tissue tension, but Burch and Sodeman¹⁵ showed that the tissue in developing edema was unusually high due to the tone of the connective tissue.

Landis³⁹ has shown that the blood pressure at the arteriolar end of the capillary loop is about 45 cm. water, that at the venous end is 22 cm. water, and that the colloid osmotic pressure of the blood is 36 cm. water. Thus, there is a tendency for ultrafiltration at the arterial end and a tendency to reabsorption of fluid at the venous end of the loop. That this ideal system operates only under "normal" conditions is well accepted. In inflammation or venous engorgement there is outpouring of filtrate into the tissue spaces. Some investigators have even assumed a linear relationship between rate of edema formation and difference between capillary pressure and the osmotic pressure of the plasma proteins.

The factors influencing the local formation of edema have been subjected to the most rigid investigations by competent observers, and it appears that the primary factors are (1) elevated capillary pressure, (2) lowered colloid osmotic pressure of the blood plasma, (3) damage to

the capillary wall, and (4) lymphatic obstruction. Contributory factors are (5) low tissue pressure, and (6) warmth. Krogh laid great stress on the intracapillary pressure, while Schade believed that the two most important balancing factors are the tissue tension ("Gewebsspannung") and the imbibition pressure of the interstitial colloids ("extracelluläre wasserdurchtränkte Bindegewebskolloid").

Drinker and Field²⁵ observed that edema fluid may contain as much as 4.5 per cent protein, and I have found blister fluid in experimentally produced burns to contain as much as 6 per cent protein, which would amount to 40 cm. water colloid osmotic pressure. Therefore, the tissue fluid may raise the osmotic pressure on the outside of the capillary to such a level that reabsorption of fluid by the capillary through osmotic means may be greatly slowed or even stopped. Specific gravity values for edema fluid corresponding to those I obtained have been found by Schade and others.

The subcutaneous pressures which were obtained in normal individuals correspond to the few recorded in the literature (Wells⁶⁵). The tensions found in inflammations were always higher than normal, tending to limit capillary filtration (Beecher⁷). In addition, it may be observed that the tissue tensions in the normal extremities of individuals with immobilized infected extremities are higher than the average "normal." This is probably due to the double duty required of the remaining mobile extremity.

Fahr²⁷ has also stated that the sum of serum protein osmotic pressure and tissue tension need not equal the sum of edema fluid osmotic pressure and intracapillary pressure except in a state of equilibrium. If fluid is leaving the capillary, the hydrostatic capillary pressure will be so high that the sum of capillary pressure and edema fluid osmotic pressure will be greater than the first sum.

In our experiments (Table XIV), it may be seen that an equilibrium exists between the forces "pulling" water into the capillary and those "pulling" water into the tissues. For example, in terms of millimeters of mercury, in animal a:

$$\begin{array}{l} \text{Force pulling water into blood:} \\ 18 \text{ (6\% plasma protein)} + 31 \text{ (tissue pressure)} = 49 \text{ mm. Hg} \\ \text{Force pulling water into tissues:} \\ 12 \text{ (4\% edema fluid protein)} + 40 \text{ (capillary pressure)} = 52 \text{ mm. Hg} \end{array}$$

In this animal, there is a definite preponderance of forces tending to put fluid into the tissues, as one might expect during edema formation.

At the beginning of this century, medical men generally looked hopefully forward to an immunologic specific for every bacterial disease. Unfortunately, however, such specifics are still too few. A surgeon still has no reliable immunologic agents upon which he may depend in the treatment of suppurations. The patient must still fight out the conflict with bacteria with little specific help from chemical irrigating

solutions, and the surgeon must content himself with supporting the natural local and general resistance of the patient in his combat with the invading bacteria. Hirschfelder has shown that no antiseptic agent will penetrate tissue effectively and preserve its antiseptic properties for more than a millimeter.

The relief of pain which attends elevation and rigid immobilization is usually striking. In the last few years, therefore, immobilization and elevation of the infected extremity in plaster have been employed as the primary treatment in a number of acute infections, among which have been cases of infection of joints, bones, and soft tissue. The remote results in the treatment of osteomyelitis, of course, cannot be definitely assayed. The impression has been gained that this method of treating joint infections, when accompanied by proper incision to afford dependent drainage of abscesses, is far superior to the method of active mobilization. Usually, the results attending its use in infections of the soft tissues are superior to those obtained by other means.

CONCLUSIONS

1. Blood flow in an extremity is definitely influenced by its position. This is shown by the fact that (a) elevation reduces the arterial systolic pressure and skin surface temperatures, and (b) dependency increases the arterial systolic pressure and skin surface temperatures.

2. The edema fluid in inflamed extremities of patients is usually under a tension higher than the venous pressure, and often higher than mid-capillary pressure. This entails an elevation of ten to twenty times the normal tissue tension and tends to effect further formation of edema fluid.

3. Immobilization and rest definitely reduce the tissue tension of an inflamed extremity.

4. The elevated skin surface temperatures of inflamed extremities is a criterion of the greater blood flow.

5. In normal young men, gravity may increase the leg volume 2 to 7 per cent during the day. In inflammations of an extremity, the volume may increase as much as 50 per cent.

6. The increased volume of an inflamed extremity can be markedly reduced by elevation.

7. The protein level of edema fluid from inflamed extremities in patients is usually just below that of the plasma and may be as high.

8. Inflammation of an extremity in the rabbit rapidly stimulates the production of edema fluid, frequently approximating in quantity the normal blood volume.

9. The edema fluid protein levels in inflamed extremities in animals approach the blood plasma levels.

10. Heat inflammation in the rabbit effects a rapid drop in the plasma proteins.

11. The edema fluid pressure in experimental inflammation rises rapidly to capillary pressure levels.

12. Capillary blood pressure is increased in the inflammatory site so that there tends to be an equilibrium between;

$$\text{tissue oncotic pressure} + \text{capillary pressure} = \text{plasma oncotic pressure} + \text{tissue pressure}$$

However, the factors on the left of the equation are relatively weighted so that there is a continuous tendency for edema formation.

13. Treatment of infections of the extremities in the University of Minnesota Hospitals over the six-year period, 1934-1939, by immobilization in casts, usually with elevation, gave good results in 72.2 per cent, fair results in 21.6 per cent, and poor results in 6.0 per cent of the cases. Chronic osteomyelitis constituted 48.3 per cent of the cases.

14. Clinical trial suggests that immobilization and elevation are adjunct measures of distinct value in supporting the natural defense mechanisms of the body in inflammations of the extremities. Their use appears to rest on a rational physiologic basis.

REFERENCES

1. Abramson, H. A.: The Mechanism of the Inflammatory Process. I. The Electrophoresis of the Blood Cells of the Horse and Its Relation to Leucocyte Emigration, *J. Exper. Med.* 46: 987, 1927.
II. Concerning the Adhesive Force of One Pseudopod of a Frog Leucocyte and Its Relation to Leucocyte Emigration, *J. Exper. Med.* 46: 1003, 1927.
The Mechanism of the Inflammatory Process. Electrophoretic Migration of Inert Particles and Blood Cells in Gelatin Sols and Gels With Reference to Leucocyte Emigration Through the Capillary Wall, *J. Gen. Physiol.* 11: 743, 1925.
Modification of the Northrop Kunitz Microcataphoresis Cell, *J. Gen. Physiol.* 12: 469, 1929.
The Cataphoretic Velocity of Mammalian Red Blood Cells, *J. Gen. Physiol.* 12: 711, 1929.
Electrokinetic Phenomena. III. The Isoelectric Point of Normal Sensitized Mammalian Erythrocytes, *J. Gen. Physiol.* 14: 163, 1930.
Electrokinetic Phenomena. VI. Relationship Between Electric Mobility, Charge, and Titration of Proteins, *J. Gen. Physiol.* 15: 575, 1932.
2. Adams, J. G.: Inflammation, London, 1907, Macmillan & Co.
3. Adler, I., and Meltzer, S. J.: Experimental Contribution to the Study of the Path by Which Fluids Are Carried From the Peritoneal Cavity Into the Circulation, *J. Exper. Med.* 1: 182, 1896.
4. Arnold, J.: Experimentelle Untersuchungen über die Entwicklung der Blutcapillaren bei der Keratitis vasculosa, *Virchows Arch. f. path. Anat.* 54: 1, 1872.
Über Diapedesis, *Virchows Arch. f. path. Anat.* 58: 231, 1873.
Über das Verhalten der Wandungen der Blutgefässe bei der Emigration weisser Blutkörper, *Virchows Arch. f. path. Anat.* 62: 187, 1875.
Über die Kittsubstanz der Endothelien, *Virchows Arch. f. path. Anat.* 66: 77, 1876.
Zur Kenntniss der Stoffdrüsen des Bindegewebes, *Virchows Arch. f. path. Anat.* 68: 165, 1876.
5. Adler, I., and Herbst, R.: Die Schwankungen des Fussvolumens und deren Beeinflussung, *Ztschr. f. d. ges. exper. Med.* 58: 137, 1923.
6. Hardy, H.: Über Hemmung inflammatorischer Symptome, *Skandinav. Arch. f. Physiol.* 32: 198, 1915.
7. Roessler, H. K.: Adjustment of the Flow of Tissue Fluid in the Presence of Localized Sustained High Venous Pressure as Found in Various of the Great Splanchnic System During Walking, *J. Clin. Investigation*, 16: 733, 1937.

8. Bellis, C. J.: A Rapid Method for Determining Specific Gravity of Body Fluids by the Falling Drop Principle, *J. Lab. & Clin. Med.* 26: 564, 1940.
9. Bellis, C. J., and Cook, M. M.: A Practical Thermoelectric Thermometer for Clinical Measurement of Skin Surface Temperatures, *J. Lab. & Clin. Med.* 25: 291, 1939.
10. Bellis, C. J., and Scott, F. H.: The Alteration of Protein Distribution, in Vitro, Between Corpuscles and Plasma Caused by Isosmotic and Hyperosmotic Solutions, *J. Biol. Chem.* 111: 17, 1935.
11. Bier, A.: Textbook of Hyperemia as Applied to Surgery, New York, 1909, English Translation by G. M. Blech. Rebman Co.
12. Böhm, B.: Fortgesetzte Untersuchungen über die Permeabilität der Gefäßwände, *Biochem. Ztschr.* 16: 313, 1909.
13. Böhme, A.: Ueber die Schwankungen der Serumkonzentration beim gesunden Menschen, *Deutsches Arch. f. klin. Med.* 103: 522, 1911.
14. Bruce, A. N.: Ueber die Beziehung der sensiblen Nerveineigungen zum Entzündungsvorgang, *Arch. f. exper. Path. u. Pharmacol.* 63: 424, 1910.
15. Burch, G. E., and Sodeman, W. A.: The Estimation of the Subcutaneous Tissue Pressure by a Direct Method, *J. Clin. Investigation* 16: 845, 1937.
Studies in Tissue Pressure, *Proc. Soc. Exper. Biol. & Med.* 36: 256, 1937.
A Direct Method for the Determination of Venous Pressure. Relationship of Tissue Pressure to Venous Pressure, *J. Clin. Investigation* 18: 31, 1939.
- Sodeman, W. A., and Burch, G. E.: Studies in Skin Distensibility, *Proc. Soc. Exper. Biol. & Med.* 38: 882, 1938.
- Sodeman, W. A.: Studies in the Physiology of Blood Vessels in Man. Apparatus and Methods. II. A Method for the Determination of the Volume of the Soft Tissue About the Terminal Phalanx of the Human Finger, *J. Clin. Investigation* 16: 787, 1937.
- Sodeman, W. A., Burch, G. E., and Turner, R. H.: Studies in the Physiology of Blood Vessels in Man. VI. Volume Changes in Human Finger Tip Following Sudden Venous Obstruction, *Proc. Soc. Exper. Biol. & Med.* 36: 259, 1937.
16. Burton, A. C.: The Measurement of Blood Flow, Venous Pressure, and Distensibility of the Digital Vessels, *Proc. Am. Physiol. Soc.* 1938, *Am. J. Physiol.* 123: 29, 1938.
17. Carrier, E. B., and Rehberg, P. B.: Capillary and Venous Pressure in Man, *Skandinav. Arch. f. Physiol.* 44: 20, 1923.
18. Chambers, R.: The Microvivisection Method, *Biol. Bull.* 34: 121, 1918.
New Apparatus and Methods for the Dissection and Injection of Living Cells, *J. Roy. Micr. Soc.*, 373, 1922.
19. Churchhill, E. D., Hakazawa, F., and Drinker, C. K. The Circulation of Body Fluids in the Frog, *J. Physiol.* 63: 304, 1927.
20. Clark, E. R.: Observations on Living Growing Lymphatics in the Tail of the Frog Larva, *Anat. Rec.* 3: 183, 1909.
Arterio-venous Anastomoses, *Physiol. Rev.* 18: 229, 1938.
- Clark, E. R., and Clark, E. L.: A Study of the Reaction of Lymphatic Endothelium and of Leucocytes in the Tadpole's Tail Toward Injected Fat, *Anat. Rec.* 11: 342, 1917.
Observations on Living Preformed Blood Vessels as Seen in Transparent Chamber Inserted Into the Rabbit's Ear, *Am. J. Anat.* 49: 441, 1932.
21. Cohnheim, J.: Ueber Entzündung und Eiterung, *Virchows Arch. f. path. Anat.* 40: 1, 1867.
Lectures on General Pathology, Vol. III, Section VI, London, 1890, The New Sydenham Society.
22. Concklin, R. E.: The Formation and Circulation of Lymph in the Frog. I. The Rate of Lymph Production, *Am. J. Physiol.* 95: 79, 1930.
III. The Permeability of Capillaries to Protein, *Am. J. Physiol.* 95: 98, 1930.
23. Dale, H. H.: The Activity of the Capillary Blood Vessels, *Brit. M. J.* 1: 959, 1923.
Progress in Autopharmacology, *Bull. Johns Hopkins Hosp.* 53: 297, 1932.
- Dale, H. H., and Laidlaw, P. P.: Further Observations on the Action of Beta Iminazolethylamine, *J. Physiol.* 43: 182, 1912.
- Dale, H. H., and Richards, A. N.: The Vasodilator Action of Histamine and of Some Other Substances, *J. Physiol.* 52: 110, 1919.
24. Dennis, F. S.: Treatment of Compound Fractures. 151 Cases Without a Death From Septic Infection, and 100 Cases With No Death From Any Cause, *J. A. M. A.* 2: 673, 1884.

25. Drinker, C. K.: The Permeability and Diameter of the Capillaries in the Web of the Brown Frog (*R. temporaria*) When Perfused With Solutions Containing Pituitary Extract and Horse Serum, *J. Physiol.* 63: 249, 1927.
The Functional Significance of the Lymphatic System, Harvey Lectures, Baltimore, 1937-38, Williams & Wilkins Company, p. 89.
- Drinker, C. K., and Field, M. E.: Lymphatics, Lymph, and Tissue Fluid, Baltimore, 1933, Williams & Wilkins Company.
- Drinker, C. K., Field, M. E., Ward, H. K., and Lyons, C.: Increased Susceptibility to Local Infection Following Blockage to Lymph Drainage, *Am. J. Physiol.* 112: 74, 1935.
- Drinker, C. K., and Field, M. E.: The Permeability of the Capillaries of the Dog to Protein, *Am. J. Physiol.* 97: 40, 1931.
- Field, M. E., and Drinker, C. K.: The Passage of Visible Particles Through the Walls of Blood Capillaries and Into the Lymph Stream, *Am. J. Physiol.* 116: 597, 1936.
- Field, M. E., Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation, *J. Exper. Med.* 56: 363, 1932.
- Field, M. E., Leigh, O. C., Heim, J. W., and Drinker, C. K.: The Protein Content and Osmotic Pressure of Blood Serum and Lymph From Various Sources in the Dog, *Am. J. Physiol.* 110: 174, 1934.
26. Drury, A. N., and Jones, N. W.: Observations Upon the Rate at Which Oedema Forms When the Veins of the Human Limb Are Congested, *Heart* 14: 55, 1927.
27. Fahr, G. E.: Personal Communication.
28. Falk, I. S., Gussin, H. A., and Jacobson, M. A.: Studies on Respiratory Diseases. XXXI. Electrophoretic Potential and Virulence of Pneumococci, *J. Infect. Dis.* 37: 481, 1925.
- Falk, I. S., Jensen, L. B., and Mills, J. H.: Simplified Electrical Method to Distinguish Toxicogenic From Non-toxicogenic Diphtheria Bacilli, *Proc. Soc. Exper. Biol. & Med.* 25: 248, 1928.
- Falk, I. S., Tonney, F. O., White, J. L., and Jensen, L. B.: Electrical Determination of Virulence on Diphtheria Cultures, *Am. J. Pub. Health* 17: 714, 1927.
- Jacobson, M. A., and Falk, I. S.: Studies on Respiratory Diseases. XIX. The Influence of Anti-serum and of Animal Passage Upon the Virulence and Electrophoresis of Pneumococci, *J. Bact.* 13: 191, 1927.
- Jensen, L. B., Falk, I. S., Tonney, F. O., and White, J. L.: Electrophoresis of Diphtheria Bacilli. II. Micro-electrophoresis and the Differentiation of Virulent, and Non-virulent Diphtheria Bacilli, *J. Bact.* 15: 413, 1928.
29. Findlay, G. M.: Histamine and Infection, *J. Path. & Bact.* 31: 633, 1923.
30. Fischer, M.: Oedema and Nephritis, New York, 1879, John Wiley & Sons, Inc.
- The Nature and the Cause of Edema, *J. A. M. A.* 51: 830, 1908.
31. Friedrich, P.: Experimentelle Beiträge zur Frage nach der Bedeutung 1. der Luftinfection für die Wundbehandlung 2. des innergeweblichen Druckes für das Zustandekommen der Wundinfection, *Arch. f. klin. Chir.* 59: 458, 1899.
32. Gaskell, W. H.: On the Tonicity of the Heart and Blood Vessels, *J. Physiol.* 3: 48, 1880.
33. Graham, T.: Liquid Diffusion Applied to Analysis, *Phil. Tr., Roy. Soc., Lond.* 151: 183, 1861.
34. Harrop, G. A. Jr., and Waterfield, R. L.: The Effect of Posture on the Composition and Volume of the Blood and on Its Selective Diffusion Into the Lymph Spaces, *J. Physiol.* 70: 32, 1930.
35. Harvey, W.: Anatomical Studies on the Motion of the Heart and Blood, Springfield, Translated by C. D. Lenke, Charles C Thomas, Publisher.
36. Hilton, J.: Rest and Pain, London, 1898, G. Bell and Sons.
37. Kanavel, A. B.: Infections of the Hand, Philadelphia, 1910, Lea & Febiger.
38. Landerer, R.: Cited by Landis and Gibson.
39. Landis, E. M.: The Capillary Pressure in Frog Mesentery as Determined by Micro injection Methods, *Am. J. Physiol.* 75: 518, 1926.
11. The Relation Between Capillary Pressure and the Rate at Which Fluid Passes Through the Walls of Single Capillaries, *Am. J. Physiol.* 82: 217, 1927.
- Micro injection Studies of Capillary Blood Pressure in Human Skin, *Heart* 15: 209, 1930.
- The Capillary Blood Pressure in Mammalian Mesentery as Determined by the Micro injection Method, *Am. J. Physiol.* 93: 353, 1930.
- Capillary Pressure and Capillary Permeability, *Physiol. Rev.* 14: 40, 1934.

- The Passage of Fluid Through the Capillary Wall, Harvey Lectures, Baltimore, 1936-37, Williams & Wilkins Company.
- Landis, E. M., and Gibbon, J. H., Jr.: Effects of Temperature and of Tissue Pressure on the Movement of Fluid Through the Human Capillary Wall, J. Clin. Investigation 12: 105, 1933.
- Landis, E. M., Jonas, L., Angevine, M., and Erb, W.: The Passage of Fluid Through the Human Capillary Wall During Venous Congestion, J. Clin. Investigation 11: 717, 1932.
40. Lewis, T.: Observations Upon the Regulation of Blood Flow Through the Capillaries of the Human Skin, Heart 13: 1, 1926.
- The Blood Vessels of the Human Skin and Their Responses, London, 1927, Shaw & Sons, Ltd.
- Lewis, T., and Grant, R. T.: Vascular Reactions of the Skin to Injury. II. The Liberation of a Histamine-like Substance in Injured Skin; the Underlying Cause of Pruritic Urticaria and of Wheals Produced by Burning, and Observations Upon the Nervous Control of Certain Skin Reactions, Heart 11: 209, 1924.
41. Lombard, W. P.: The Blood Pressure in the Arterioles, Capillaries, and Small Veins of the Human Skin, Am. J. Physiol. 29: 335, 1912.
42. Magnus, R.: Ueber die Entstehung der Hautödeme bei experimenteller hydroämischer Plethora, Arch. f. exper. Path. u. Pharmacol. 42: 250, 1899.
43. McMaster, P. D.: Changes in the Cutaneous Lymphatics of Human Beings and in the Lymph Flow Under Normal and Pathological Conditions, J. Exper. Med. 65: 347, 1937.
- McMaster, P. D., and Hudack, S. S.: The Permeability of the Lymphatic Wall, Proc. Soc. Exper. Biol. & Med. 28: 852, 1931.
- The Participation of Skin Lymphatics in Repair of the Lesions Due to Incisions and Burns, Proc. Soc. Exper. Biol. & Med. 60: 479, 1934.
- The Permeability of the Wall of the Lymphatic Capillary, Proc. Soc. Exper. Biol. & Med. 56: 223, 1932.
- McMaster, P. D., Hudack, S., and Rous, P.: The Relation of Hydrostatic Pressure to the Gradient of Capillary Permeability, Proc. Soc. Exper. Biol. & Med. 55: 203, 1932.
- McMaster, P. D., and Parsons, R. J.: The Effect of the Pulse on the Spread of Substances Through Tissues, Proc. Soc. Exper. Biol. & Med. 68: 377, 1938.
- Hudack, S. S., and McMaster, P. D.: Normal and Pathological Permeability of the Lymphatic Capillaries in Human Skin, Proc. Soc. Exper. Biol. & Med. 29: 944, 1932.
- Parsons, R. J., and McMaster, P. D.: The Effect of the Pulse Upon the Formation and Flow of Lymph, J. Exper. Med. 68: 353, 1938.
44. Mende, D.: Ueber Hyperämie und Ödem bei der Hemmung der Rückflusses des venösen Blutes durch die Staubinde, Deutsche Ztschr. f. Chir. 150: 379, 1919.
45. Meyer, P.: Untersuchungen über den kolloidosmotischen Druck des Blutes. I. Ödem und Ödemausschwemmung, Ztschr. f. klin. Med. 115: 647, 1931.
46. Odermatt, W.: Die Schmerzempfindlichkeit der Blutgefäße und die Gefäßreflexe, Beitr. z. klin. Chir. 127: 1, 1922.
47. Opie, E. L.: Inflammation, Arch. Int. Med. 5: 541, 1910.
48. Orr, H. W.: The Treatment of Osteomyelitis and Other Infected Wounds by Drainage and Rest, Surg., Gynec. & Obst. 45: 446, 1927.
49. Peters, J. P.: Distribution and Movement of Water and Solutes in the Human Body, Yale J. Biol. & Med. 5: 431, 1933.
50. Plass, E. D., and Rourke, M. D.: The Effect of Venous Stasis on the Proteins of Blood Plasma and on the Rate of Sedimentation of the Red Blood Corpuscles, J. Lab. & Clin. Med. 12: 735, 1927.
51. Reiss, E.: Die refraktometrische Blutuntersuchung und ihre Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. 10: 531, 1913.
52. Ricker, G., and Regendanz, P.: Beiträge zur Kenntnis der örtlichen Kreislaufstörungen, Virchows. Arch. f. path. Anat. 231: 1, 1921.
53. Rosenbach, O.: Warum und in welchen Grenzen sind anästhetisierende Mittel bei entzündlichen Prozessen wirksam, München. med. Wehnschr. 18: 857, 1906.
54. Rowe, A. H.: The Effect of Venous Stasis on the Proteins of Human Blood Serum, J. Lab. & Clin. Med. 1: 485, 1916.
55. Schade, H.: II. Das Quellungsvermögen des Bindegewebes in der Mannigfaltigkeit seiner Erscheinungen, Ztschr. f. exper. Path. u. Therap. 14: 1, 1913.
- Gewebselastometrie zu klinischem und allgemeinärztlichem Gebrauch, München. med. Wehnschr. 73: 2241, 1926.

- Schade, H., Claussen, F., Häbler, G., Hoff, F., Mochizuki, N., and Birner, M.: Weitere Untersuchungen zur Molekularpathologie der Entzündung. Die Exsudate, *Ztschr. f. d. ges. exper. Med.* 49: 334, 1926.
56. Spiess, G.: Die Heilwirkung der Anästhetica, *Centralbl. f. innere Med.* 222: 23, 1902.
- Therapeutische Versuche zur Heilung von Krebgeschwülsten durch die Methode der Anästhesierung, *München. med. Wchnschr.* 40: 1948, 1906.
57. Starling, E. H.: The Influence of Mechanical Factors on Lymph Production, *J. Physiol.* 16: 224, 1894.
- On the Absorption of Fluid From the Connective Tissue Spaces, *J. Physiol.* 19: 312, 1896.
- The Fluids of the Body, London, 1909, Constable & Co., Ltd.
58. Stead, E. A., and Kunkel, P.: A Plethysmographic Method for the Quantitative Measurement of the Blood Flow in the Foot, *J. Clin. Investigation* 17: 711, 1938.
59. Strax, P., and deGraff, A. C.: A New Method for Clinical Determination of Human Capillary Tension, *Am. Heart J.* 6: 807, 1931.
60. Thompson, W. O., Thompson, P. K., and Daily, M. E.: The Effect of Posture Upon the Composition and Volume of the Blood in Man, *J. Clin. Investigation* 5: 573, 1928.
61. Turner, R. H.: Studies in the Physiology of Blood Vessels in Man. Apparatus and Methods. I. A Sensitive Plethysmograph for a Portion of the Finger, *J. Clin. Investigation* 16: 777, 1937.
62. Underhill, F. P., Kapsinow, R., and Pack, G. T.: Blood Concentration C. Superficial Burns, and Their Significance for Systemic Treatment, *Arch. Int. Med.* 32: 31, 1923.
- Underhill, F. P., Kapsinow, R., and Fisk, M. E.: Changes in Capillary Permeability Induced by a Superficial Burn, *Am. J. Physiol.* 95: 315, 1930.
- The Extent of Edema Fluid Formation Induced by a Superficial Burn, *Am. J. Physiol.* 95: 325, 1930.
63. Wangenstein, O. H.: Anti- or Prophlogistic Treatment of Acute Infections? The Role of Immobilization and Elevation in Pyogenic Infections of the Extremities, *Surgey* 4: 140, 1938.
- The Importance of Immobilization and Posture in the Treatment of Acute Infections of the Extremities, *Minnesota Med.* 21: 225, 1938.
- The Surgeon's Role in the Treatment of Infections, *Wisconsin M. J.* 37: 629, 1938.
64. Waterfield, R. L.: The Effects of Posture on the Circulating Blood Volume, *J. Physiol.* 72: 110, 1931.
65. Wells, H. S.: The Concentration and Osmotic Pressure of the Proteins in Blood Serum and in Lymph From the Lacteals of Dogs, *Am. J. Physiol.* 101: 421, 1932.
- Wells, H. S., Youmans, J. B., and Miller, D. G.: Tissue Pressure (Intracutaneous, Subcutaneous, and Intramuscular) as Related to Venous Pressure, Capillary Filtration, and Other Factors, *J. Clin. Investigation* 17: 489, 1938.
66. White, B. V., and Jones, C. M.: The Rate of Filtration Through the Capillary Walls as Measured by the Pressure Plethysmograph. Observations on Control Subjects and on Patients With Intrahepatic Disease, Thyrotoxicosis, and Myxedema, *J. Exper. Med.* 18: 73, 1939.
67. Youmans, J. B.: Certain Factors Influencing the Exchange of Fluid Between the Blood and the Tissues, and Their Relation to the Occurrence of Edema in Patients, *Tr. A. Am. Physicians* 50: 118, 1935.
- Youmans, J. B., Akroyd, J. H., and Frank, H.: Changes in the Blood and Circulation With Changes in Posture. The Effect of Exercise and Vasodilatation, *J. Clin. Investigation* 14: 739, 1935.
- Youmans, J. B., Wells, H. P., Donley, D., and Miller, D. G.: The Effects of Posture (Standing) on the Serum Protein Concentration and Colloid Osmotic Pressure of Blood From the Foot in Relation to the Formation of Edema, *J. Clin. Investigation* 12: 965, 1933.

RESUSCITATION IN ADVANCED ASPHYXIA

ROLE OF POSITIVE AND NEGATIVE PRESSURE

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INTRODUCTION

ACUTE asphyxia is generally considered to progress in four, more or less, definite phases³:

1. *The period of primary apnea*, in which the breath is held, the glottis may or may not be closed in spasm, and a period of shallow breathing may ensue.

2. *The period of dyspnea*, in which the respiratory movements are greatly increased, the accessory muscles of respiration come into play, tonic and clonic convulsions may appear, and the blood pressure rises.

3. *The period of terminal apnea*, in which the respiration has ceased; in exceptional cases, some asphyxial or agonal gasps may be taken. The limbs become limp, the blood pressure falls, but the heartbeat is still definite and regular. For the first part of this period, the heart rate may increase and the pulse pressure decrease. Toward the end of the period, the heart generally becomes slower and irregular, although the pulse may increase. The pupils are dilated and their reflexes gone; the corneas are glassy. Defecation and micturition may occur. At the end of this period the heart rate may again increase, its output diminish, and it is difficult to tell whether the heartbeats are expulsive.

4. *The period of failure of the heart*, in which the heart may fail either in standstill or in ventricular fibrillation (Fig. 1), and death occurs.

In general, each period lasts about a minute. Considerable variation, however, may occur in the time periods and in the characteristics of each phase of asphyxia, especially when an anesthetic has been administered before the start of the experiment.

MODES OF PRODUCTION OF ASPHYXIA

In these experiments, asphyxia was produced either by (1) mechanical obstruction of a face mask or obstruction of an intratracheal tube, or (2) inhalation of inert gases (nitrogen, helium, or nitrous oxide) at the mask or by way of the intratracheal tube, with an inflatable rubber cuff to avoid leakage.

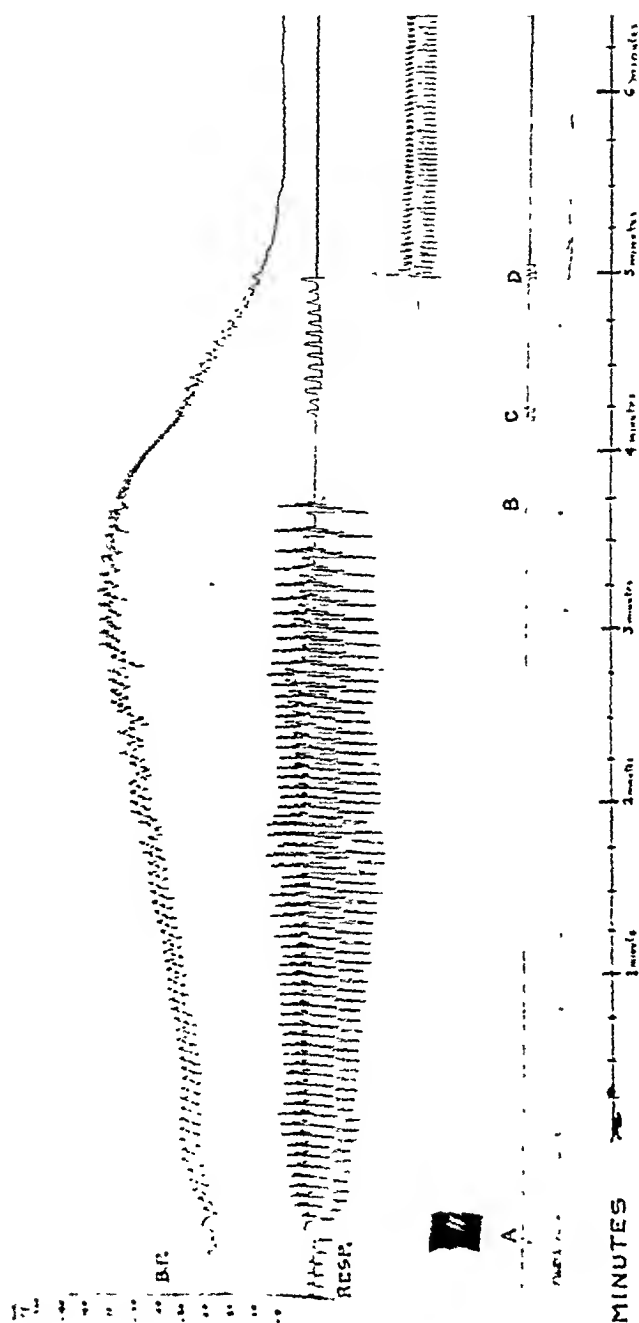


FIG. 1 (Dog 1D).—Mechanical obstruction asphyxia at the mask. A, Obstruction at mask begun; B, respiration ceases; C, manual artificial respiration with O₂ started, but was ineffectual; D, resuscitator with oxygen started but this, too, was ineffectual at this point.

EVIDENCE OF RESUSCITATION

Resuscitation procedures were carried out by way of the face mask or intratracheal tube. The criteria of successful resuscitation were (1) rapid rise of the blood pressure which was maintained and (2) a return of regular respiration (Fig. 2).

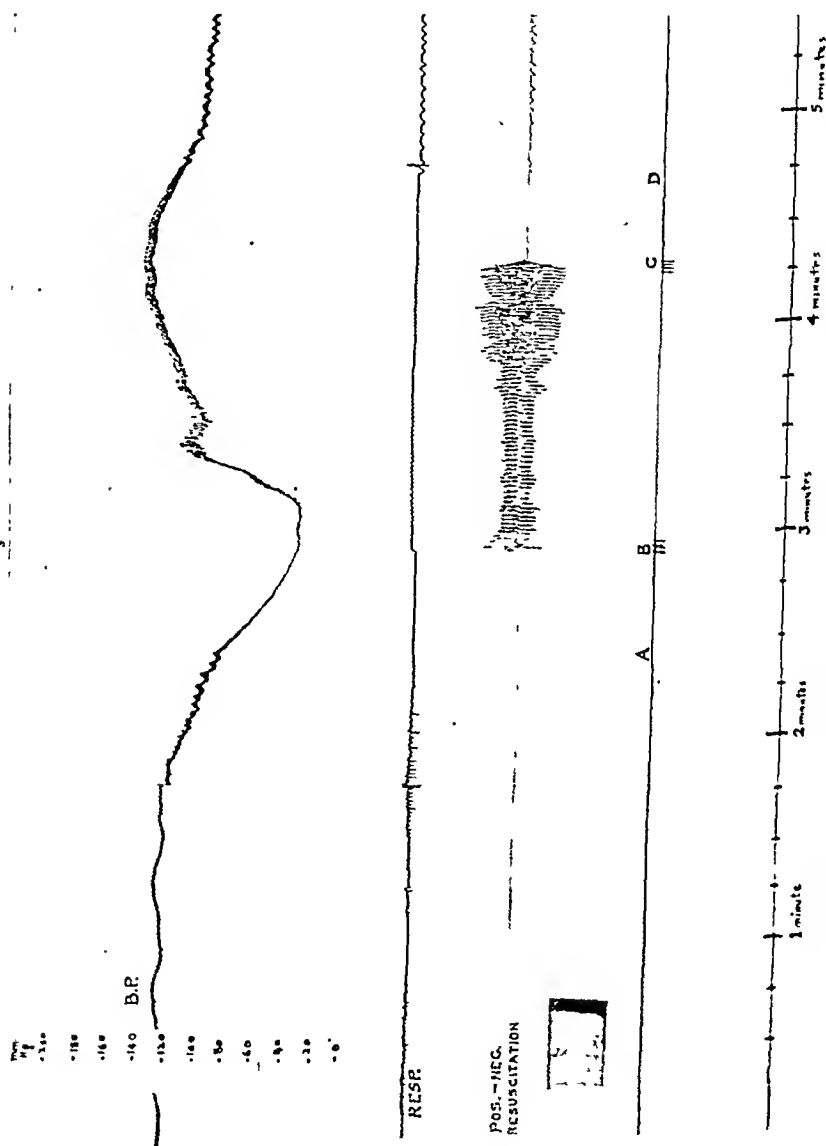


Fig. 2 (Dog 5).—Nitrogen inhalation asphyxia at the mask. A, Respiration ceases; B, resuscitator with oxygen started; C, resuscitator discontinued, mask opened to atmosphere; D, spontaneous respiration ensues.

DISCUSSION

In our experiments on animals (dogs), four methods of resuscitation were used:

1. Manual artificial respiration with inhalation of oxygen was carried out by moderately vigorous, side-to-side compression of the lower thorax

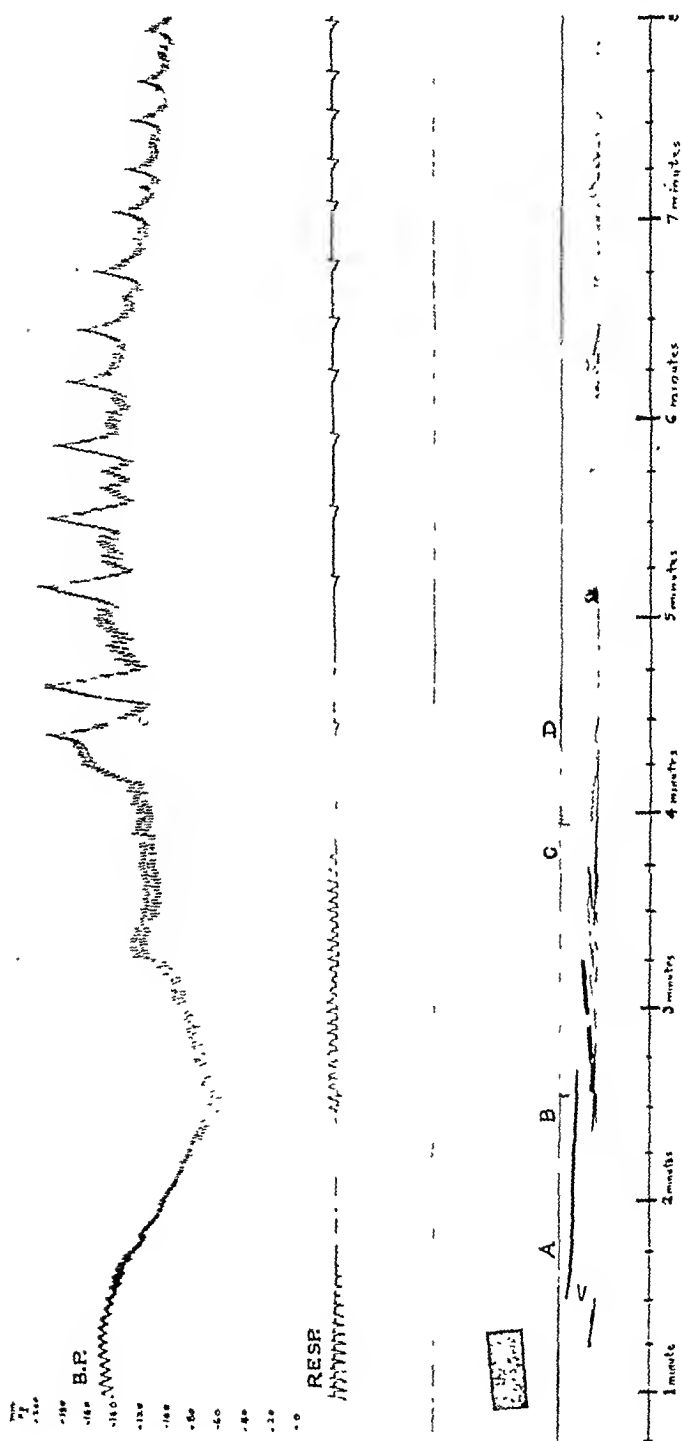


Fig. 3 (Dog 13).—Nitrous oxide asphyxia at the mask. *A*, Respiration ceases; *B* and *C*, manual artificial respiration with oxygen, showing slow recovery of blood pressure; *D*, spontaneous respiration.

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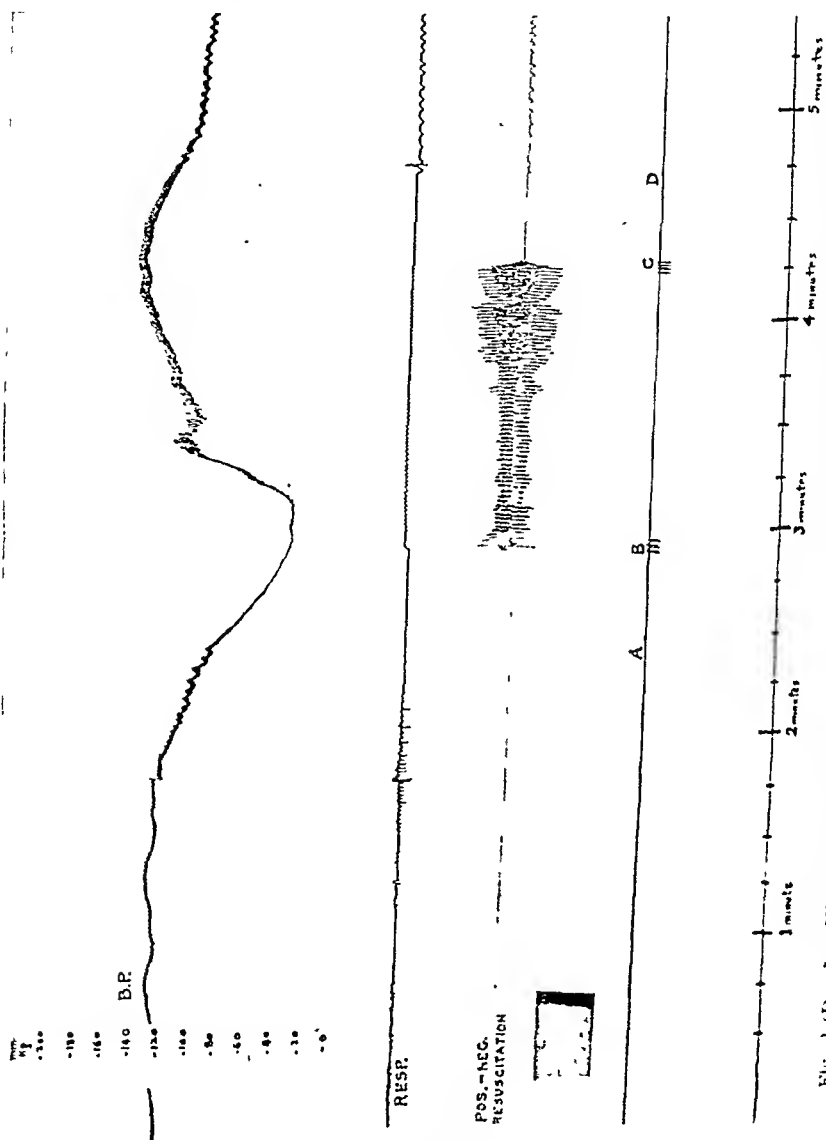


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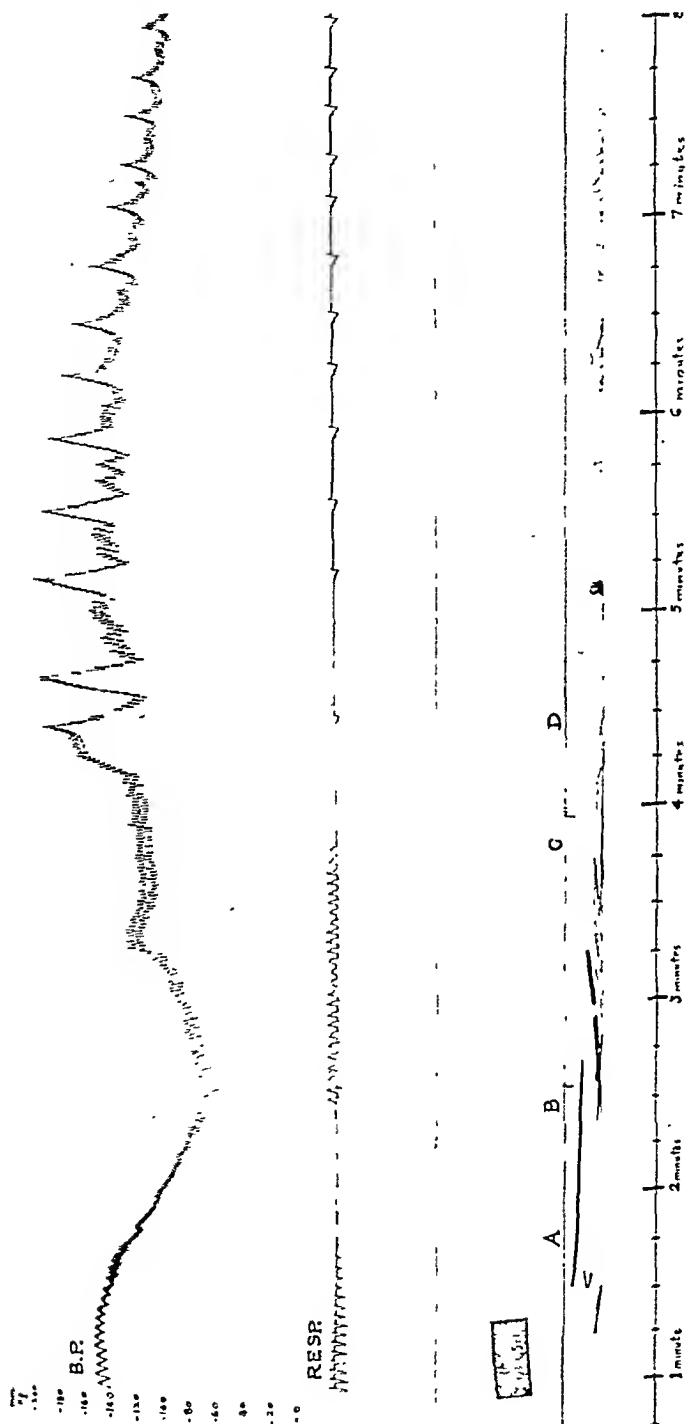


Fig. 3 (Dog 13).—Nitrous oxide asphyxia at the mask. *A*, Respiration ceases; *B* and *C*, manual artificial respiration with oxygen, showing slow recovery of blood pressure; *D*, spontaneous respiration.

by the extended fingers of both hands at the same time the thumbs and thenar eminences of the hands compressed the upper abdomen.

2. The rhythmic inflation of oxygen was carried out at 12 to 15 mm. Hg pressure.

3. Rhythmic suction with oxygen was carried out at 8 to 12 mm. Hg pressure.

4. Mechanical resuscitation* was carried out with rhythmic alternating pressure and suction of +14 mm. Hg and -9 mm. Hg, with oxygen.

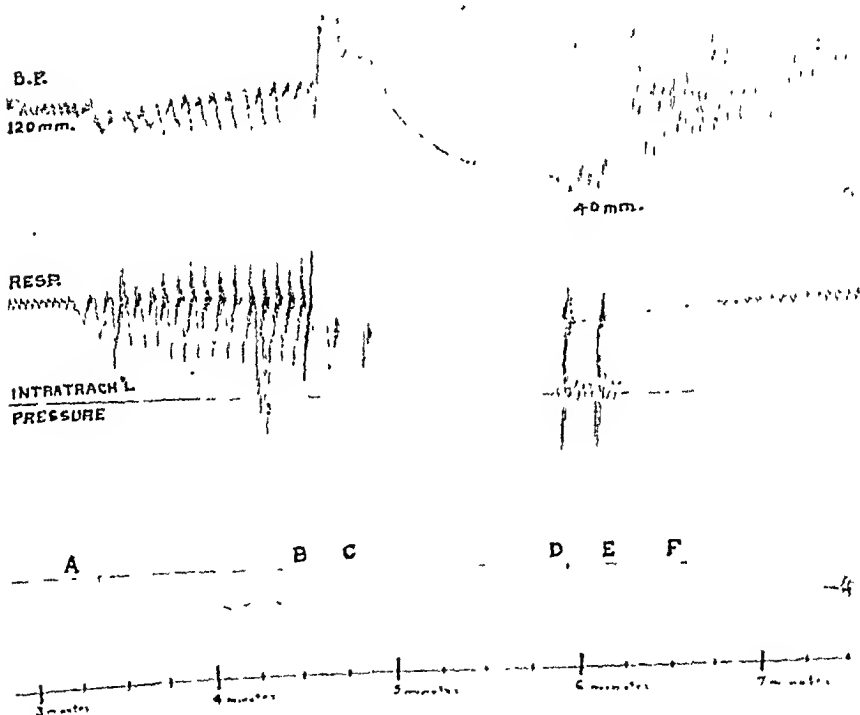


Fig. 1 (Dog 16).—Mechanical obstruction asphyxia at intratracheal tube. A, Obstruction of tracheal tube; B, drum stopped to conserve space; C, respiration ceases; D and E, rhythmic inflation of oxygen (14 mm Hg to 0 mm Hg), notice the immediate stimulation of the respiratory mechanism as evidenced by the greatly increased height of the intratracheal pressure curve; F, spontaneous respiration begins.

Table I (left half, oxygen) shows the degree of success obtained by the various methods. It is seen that manual artificial respiration with oxygen inhalation was successful in 55 per cent of the experiments. Rhythmic inflation with oxygen was successful in 78 per cent, rhythmic

*Emerson resuscitator.

rhythmic inflation and suction is even more valuable, as can be seen in Table I.

The value of the resuscitation procedure alone without the stimulating effect of oxygen can be demonstrated by attempting to resuscitate with an inert gas instead of oxygen. We have called this resuscitation the Phenomenon of Asphyxial Resuscitation (Fig. 6). It can be produced in a high percentage of instances only with the combination of rhythmic inflation and suction. Using nitrogen, resuscitation can be produced by manual artificial respiration in 15 per cent, by rhythmic inflation in 17 per cent, by rhythmic suction in 20 per cent, and by combined inflation and suction in 85 per cent of the instances where tried. This phenomenon cannot be produced after double vagotomy (Fig. 7).

From the above considerations it becomes clear that in advanced asphyxia with cessation of respiration, the inflation and suction action on the lungs is important in stimulating the respiratory and circulatory mechanisms.

Section of the vagi prevents the occurrence of the phenomenon of asphyxial resuscitation, although resuscitation still may be produced after double vagotomy and asphyxia by using oxygen instead of nitrogen. In the latter instance, resuscitation is accomplished by the factor of oxygen alone, and without the benefit of reflex stimuli.

We wish to emphasize that it is the combination of a reflex from active inflation and a reflex from active deflation which is necessary to produce this phenomenon.

Howell¹ states: "It was found that at each inspiration the galvanometer gave evidence of the passage of afferent nerve impulses, and that when the lungs were forcibly collapsed by active suction a record was obtained which might be accepted as evidence of the discharge of a different set of fibers. More recently a similar result has been obtained by Adrian making use of his special technique. After cutting the vagus high in the neck, he dissected the nerve so as to isolate a small group of fibers having a common origin in the lungs. These fibers were connected with an oscillograph recorder through an amplifier so that a magnified record was obtained of their activity. In this way he was able to show that at each inspiration there is a burst of afferent discharges, the rate increasing as the lungs expand and falling off, perhaps to zero, as they collapse in expiration. This result indicates that there are receptors, stretch receptors, in the lungs which are stimulated mechanically as the lungs expand and in proportion to the degree of expansion, just as the stretch receptors, the spindles, in a muscle are stimulated by stretching it. The histologic character and location of these sense endings in the lungs are still to be determined. It is believed that the afferent impulses thus aroused act to inhibit the inspiratory discharge from the respiratory center and shorten the inspiratory movement. The result is to quicken the respiratory rate, since the center recharges

PHENOMENON OF ASPHYXIAL RESUSCITATION

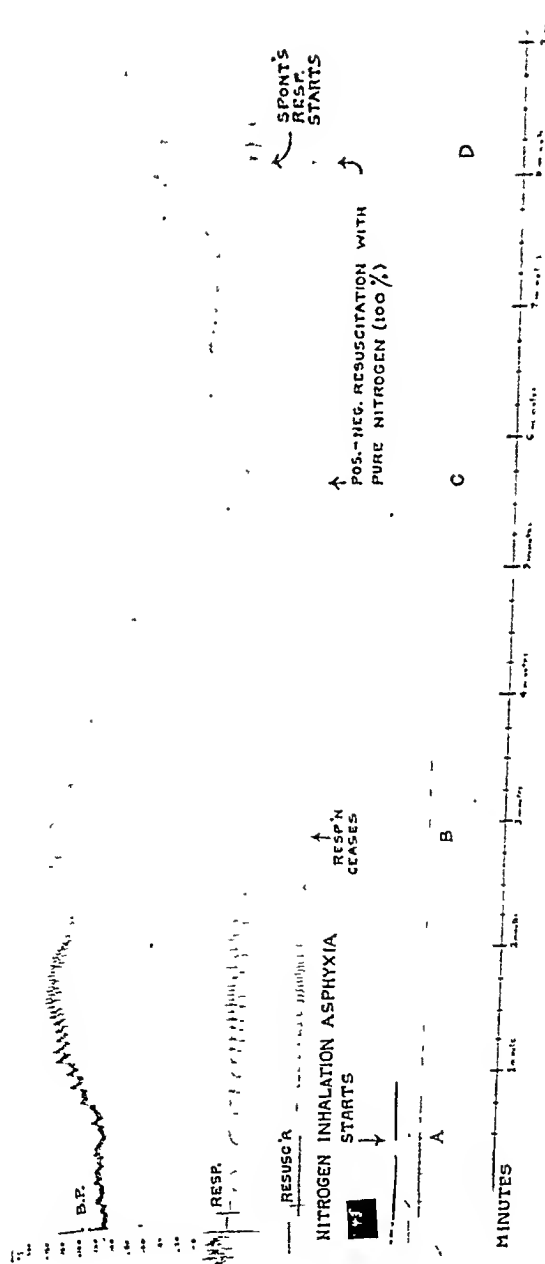


Fig. 6 (Dog 43).—Phenomenon of asphyxia resuscitation. *A*, Nitrogen inhalation asphyxia is started by way of the intratracheal tube; *B*, respiration ceases; *C*, almost 3 minutes after the respiration has ceased, pure nitrogen is administered by the suck-and-blow, resuscitator (14 mm. Hg, -9 mm. Hg), and 1½ minutes later the blood pressure starts to rise; *D*, spontaneous respiration is initiated and the intratracheal tube is opened to the atmosphere.

more promptly. The mechanism acts automatically to keep the respirations more rapid and more shallow than would otherwise be the case. It was found also by this method that a sudden suction applied to the lungs set up a burst of afferent discharges, but that this was not the case with the normal passive collapse of the lungs."

Henderson and Turner² do not see the necessity of the suction phase of resuscitation when, for example, asphyxia occurs during an operation on a patient, with the chest open, since the lung is already collapsed. However, we want to point out that there is the *contralateral* lung which is *not* collapsed, and it is principally upon this lung that the benefit of reflex resuscitation depends. This benefit becomes even more important when the chest is opened and one lung is already collapsed. In addition, the suction phase of suck-and-blow resuscitation maintains a more regular pulmonary ventilation, even in the collapsed lung.

CONCLUSIONS

1. Rhythmic inflation and rhythmic deflation (suction) of the lungs each have a very definite and valuable place in resuscitation in advanced asphyxia.

2. The combination of rhythmic inflation and deflation of the lungs with oxygen or carbogen, using safe pressures, is superior to manual artificial respiration, rhythmic inflation alone, or rhythmic suction alone.

The authors are indebted to Dr. Otis M. Cope, Professor of Physiology, and his staff, for their kind cooperation.

REFERENCES

1. Howell, William H.: Textbook of Physiology, Philadelphia, 1936, W. B. Saunders Co., pp. 735-6.
2. Henderson, Y., and Turner, J. McC.: Artificial Respiration and Inhalation: The Principle Determining the Efficiency of Various Methods, J. A. M. A. 116: 1508, 1941.
3. Coryllos, P. N.: Mechanical Resuscitation in Advanced Forms of Asphyxia: A Clinical and Experimental Study of the Different Methods of Resuscitation, Surg., Gynec. & Obst. 66: 698, 1938.

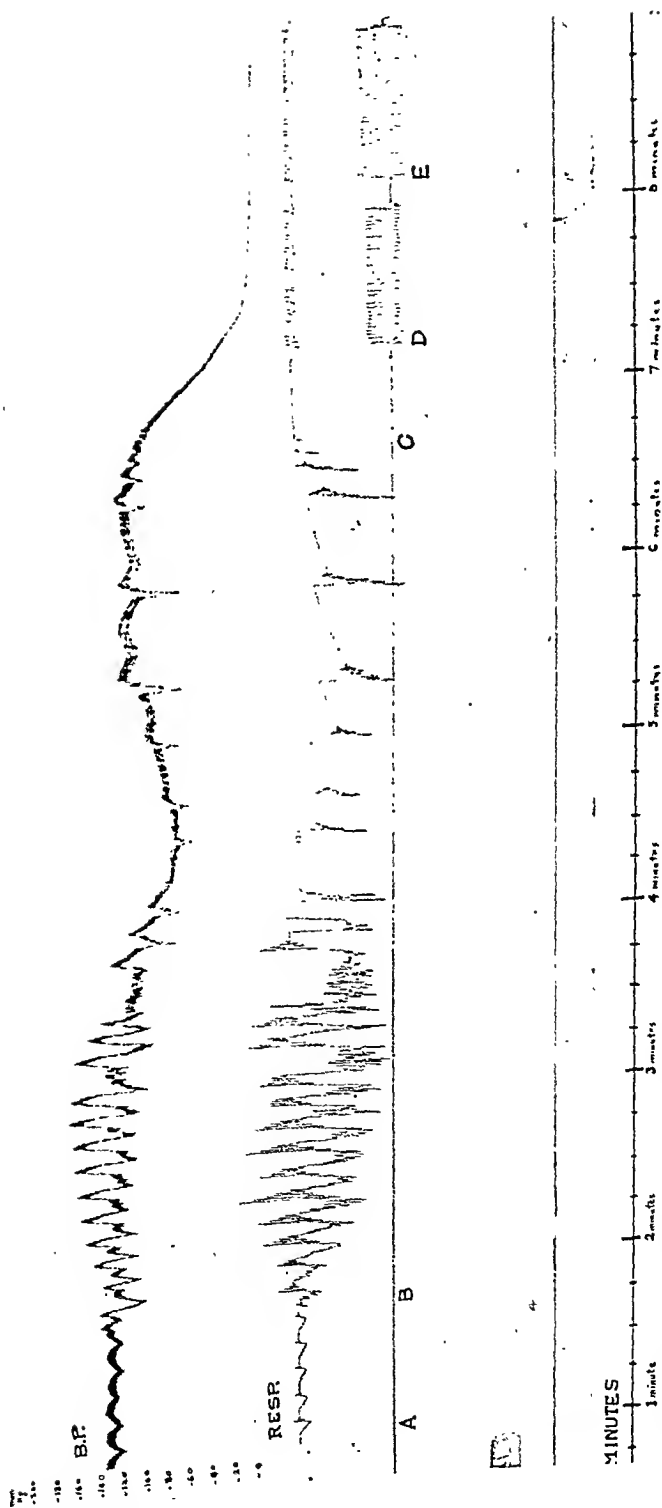


Fig. 7 (Dog 38).—Failure of phenomenon of asphyxial resuscitation after double vagotomy. A, Record taken after both vagi were cut in the mid-neck below the level of the carotid sinus; B, the intratracheal tube is clamped; C, respiration ceases and the blood pressure starts to fall precipitously, which is quite characteristic; D and E, attempts at suck-and-blow resuscitation with nitrogen fail.

In the past, assiduous attention on the part of the surgeon and all assistants was imperative to maintain proper approximation of the parts without unduly stretching the pedicle of the graft from its donor site or of the sutures at the recipient site. This extreme and tedious cooperation was a sine qua non that spelled success or failure, and to obviate this difficulty a simple form of immobilization and approximation is proposed, namely the mermaid plaster cast.

Method of Procedure.—Two days before operation the defect is inspected and approximated to a healthy area on the opposite calf, usually by crossing the legs. The donor area and pedicle are outlined with dye or silver nitrate stick. The legs are now separated without changing the comfortable angles at which the ankles and knees have been held. After applying requisite stockinet and padding, a plaster cast is applied from the upper thigh to the toes, meanwhile maintaining the original degree of angulation at the knee and ankle. A cast is likewise applied to the opposite leg. A large window is now cut out over the defect and a similar large opening made over the donor site. Through these windows the areas can be adequately prepared.

Operation.—A pedicle flap on the donor leg is incised as previously planned, with a broad base and with ample subcutaneous tissue. By crossing the casted extremities, the donor and defect sites can be approximated and their relative position maintained with ease. The pedicle is sutured in position along the distal and lateral edges, preferably with waxed silk interrupted sutures. By gentle manipulation of the casts the pedicle can be moved so as to be held sufficiently relaxed or taut as necessary. The wounds are dressed with a generous supply of vaseline gauze. If pressure is required on the pedicle in its new bed, a moistened sea sponge can be applied over the vaseline gauze (Fig. 1).

In this easy position, without danger of injury to the graft, the limbs can now be connected with a few rolls of plaster which, when set, will absolutely hold them immobile for the required time, usually from eighteen to twenty-one days. The patient is comfortable and can be turned on his side or face (Fig. 2).

Treatment of the Pedicle Graft.—At its new site, after severance and separation at the base, the properly planned pedicle will amply cover the defect. Trimming of the base and edges may be necessary so that proper application of skin edges may be secured. The edges of the three sides formerly sutured have formed a firm union in their new position. The base is now sutured in position with one or two small drains inserted. The subsequent treatment demands meticulous care because this flap is a delicate new-born, is mildly edematous, and requires constant gentle pressure which is just sufficient to prevent swelling but does not produce anemia. Mild external radiant heat is applied from a covered overhanging lamp.

ITALIAN METHOD OF PLASTIC REPAIR OF DENUDED AREAS FOLLOWED BY MERMAID CAST IMMOBILIZATION

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PATIENTS suffering from tender, healed scars of the legs or from denuded areas and ulcers of the legs of recent or remote origin comprise a considerable proportion of those odd refractory cases that, after being passed on from clinic to clinic, at long last reach the orthopedic department. Having experienced too many failures with various methods of conservative treatment, including the usual methods of skin grafting to the lower leg, a method of treatment was sought which would prove more acceptable and more efficient and would assure more successful end results.

The Italian method of skin grafting seemed to be physiologically sound and altogether the most acceptable of the various skin grafting methods. It was first described in 1442 by Brancha of Cateno, Italy, and later by Gasparri Togliacozzi, who popularized the method by publishing a book on pedicle skin grafting in 1597. This voluminous masterpiece contains many beautiful illustrations.

Grafts of various types applied to the tibial surfaces of the leg are only moderately successful and frequently fail. Failure is caused by (1) lack of sufficient bed of subcutaneous tissue; (2) local inanition of the part; (3) inflammatory conditions under which the thin or small grafts cannot survive; (4) mild local infections which destroy the delicate grafts; (5) circulatory causes, such as endarteritis obliterans, localized edema from obstruction to venous return, and capillary deficiency in surrounding scar tissue; and (6) chronic conditions in deeper tissues, such as mildly inflammatory osteomyelitis or osteitis, which constantly present obstacles to the healing of the delicate new grafts.

The advantages of the Italian method of skin grafting are (1) adequacy of size and supply, (2) assurance of viability of the graft through its broad pedicle, (3) easy adaptability to almost any location of the leg or foot, (4) sufficiency of subcutaneous tissue, (5) simplicity of procedure, (6) easy position of patient during the process, and (7) a protecting pad can be placed over bony areas. On the other hand, the disadvantages that may be given are (1) necessity of immobilization for three or four weeks, (2) two operations are necessary, (3) local mild infection with mildly offensive odor may occur, and (4) the difficulty of holding the limbs together at proper approximation for the required time.

COMMENTS

In the application of any pedicle graft certain general broad rules must be followed, but deviation from strict adherence to a rule may be necessary occasionally. To maintain nutrition of the flap from the beginning, the subcutaneous connective tissue, including the superficial fascia, must be included because, as Kirschner states, the arteries supplying the skin run in this connective tissue. Regarding nutrition of the flap, it makes little difference whether a flap be pedunculated distally



Fig. 3.—Donor site on right leg.

or proximally, but it is pedunculated proximally whenever possible. It is more important for incision lines to follow tension lines than lines of lymphatic or vascular supply. Those lines on the posterior surface of the leg run in an obliquely longitudinal direction from above and outward to below and inward. Adherence to this principle is not so essential if the flap is a broad one, but if it is a long narrow one in which the skin edges can be undermined and drawn together at the second

Treatment of the Donor Site After the Second Stage of Operation.—

Due to elastic contracture of the surrounding skin, the donor site defect may be considerably larger than the area first outlined (Fig. 3). Nevertheless, the base is of muscle and fascia with abundant blood supply. It is covered with pinch grafts from the thigh or adjacent calf. All of these usually survive and complete epithelialization of the intervening spaces occurs in less than two weeks' time (Fig. 4).

After the pedicle has been cut, the casts are removed and left off.



Fig. 1.—Pedicle graft in position before separation

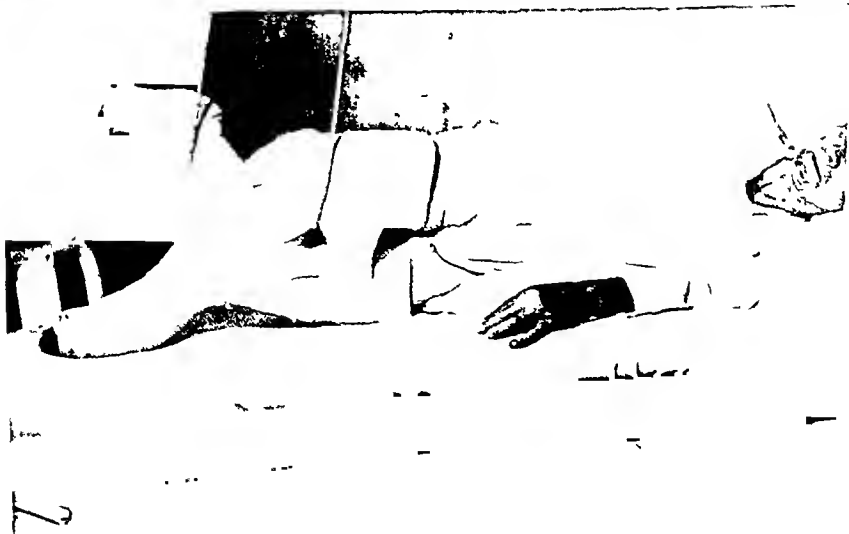


Fig. 2—Showing position of patient in bed after the first operation. Note the angulation of the legs

Denuded ulcers should be treated conservatively until there is a minimum of infection present and until the base is covered with healthy granulations.

Ulcers exposing the bone of the tibia should be treated conservatively until the bone is covered with healthy granulations.

In *scar formation over large areas of the tibia* the thin, delicate, superficial epithelial covering should be excised first so that defect edges extend to healthy surrounding tissues.

In *scars from recurrent osteomyelitis* the underlying condition as well as the underlying unhealthy bone should be treated first. The administration of sulfonamides has met with spectacularly successful results by Hoyt of Akron and their use is indicated.

Indolent ulcers with malignant tendency should be rather widely excised before grafting.

Defects of areas following compound fractures from a strictly orthopedic standpoint comprise a considerable proportion of the cases which are suitable for the proposed procedure. The recent fracture should be treated until osseous repair has been established. The nonunion may necessitate a skin graft procedure before a bone graft operation can be attempted with reasonable assurance of success.

CASE REPORTS

CASE 1.—A. M., an 18-year-old girl, was admitted to the Cook County Hospital, April 1, 1937, because of an ulceration over the internal side of the right ankle measuring 3 by 2 inches, and swelling, redness, and stiffness of the lower leg and ankle. The diagnosis was chronic ulceration of the leg due to an old healed osteomyelitis, and extensive scar formation.

Casts were applied and fenestrated as has already been described. Then the ulceration was completely excised through the surrounding scar tissue. The base of the ulcer was greatly curetted. A pedicle flap pedunculated proximally was incised on the calf area of the left leg. This extended through the skin and superficial fascia down to the deep fascia. It was lifted, the legs were crossed, and the graft approximated to the defect on the right leg. The distal and lateral edges of the graft were sutured into the corresponding edges of the defect with interrupted waxed silk sutures. A vaseline gauze dressing was applied and some soft sponges packed in to give moderate pressure. By manipulation of the casted extremities, the pedicle could be loosened the desired amount. There was no tension and circulation seemed to be adequate in the graft. In this easy position, with a few rolls of plaster of Paris, the casted extremities were immobilized.

The second stage operation was performed, April 24. At this time the base of the pedicle was severed, the legs were separated, and the casts removed. The proximal edge of the skin graft was trimmed, fitted neatly into the proximal edge of the defect, and sutured with black silk. It was found that the three edges had grown in their new position and that a portion of the base had become adherent. Pinch grafts were applied to the donor area on the calf. Vaseline gauze dressings were applied to the pedicle graft with moderate pressure, the leg elevated, and mild heat applied.

Dressings were inspected one week later and on May 8, when the dressings were changed, the graft was noted to be a 100 per cent "take." The patient was allowed up one week after this; there was slight discharge from one sinus

stage, adherence to this principle is advisable. If tension lines are followed, little evidence of scar contracture results.

The area to be incised must first be carefully and deliberately planned, always remembering that shrinkage of the pedicle takes place between the initial operation and the second stage and during the healing process in its new bed. This is more pronounced in the young. The use of a dye or silver nitrate stick to outline the proposed incision obviates haphazard guesswork at the time of operation. Excessive torsion and undue stretching of the flap should be avoided so that



Fig. 4.—Photograph showing scars from pinch grafts used to fill in donor site.

exchange of tissue fluids may be facilitated. The base of the pedicle should be broader than the outline of the flap itself so as to assure continued viability of the graft.

Preparation of the Bed.—Since there is a wide variance in the type of case suitable for pedicle skin grafting, no absolute procedure can be dogmatically laid down, but the following measures are strongly advised.

CASE 6.—R. P., a white boy, aged 9 years, was admitted to the South Shore Hospital, July 9, 1938, following an injury. He had a traumatic defect on the lower right leg measuring 4 by 2 inches. Operation was performed and pedicle skin grafts were applied through windowed casts.

Eighteen days after the initial operation the second one was done. Split thickness Thiersch grafts from the left thigh were applied to the defect in the calf and vaseline gauze dressings applied.

The postoperative course was uneventful; all the graft lived but it shrunk somewhat from the proximal suture line inserted at the second operation.



Fig. 5.—Final result; note the extension present in arm and fingers.

CASE 7.—W. G., male, aged 21 years, was admitted to the Cook County Hospital, Feb. 21, 1939, with a case of osteomyelitis for which many operations had been done. Two years previously he had had a skin graft with a mermaid cast, with excellent results. At this time he had another area of ulceration due to breaking down of the old scar at a new position. The patient was prepared and operated upon according to the technique already described. The postoperative course was uneventful; the patient tolerated the immobilization without complaint. The second operation was also performed without difficulty and the patient was discharged from the hospital April 12, 1939, with an excellent result. He was seen again in December, 1939, and the graft was found completely healed.

CONCLUSIONS

1. Denuded areas on the legs and feet present a definite problem in orthopedic clinics.
2. The Italian method of skin grafting has been found to be a relatively safe and successful procedure for their care.
3. Mermaid cast immobilization facilitates the operative procedure and the postoperative care.
4. Seven cases are presented in six patients and results illustrated by photographs.

under the graft, which subsequently closed. Since that time it has remained healed; the ulcer is covered and there is ample pad over this portion of the tibia.

CASE 2.—W. G., male, aged 19 years, was admitted to the Cook County Hospital, March 17, 1937, because of an ulceration over the middle third of the left tibia on the anterior surface, and extensive scar formation and tenderness over the middle two-thirds of the same leg. Operation was performed and mermaid casts applied as has been described. The postoperative course was uneventful and the patient tolerated the casts without any complaint.

CASE 3.—S. S., a colored man, aged 26 years, entered the Cook County Hospital, May 15, 1937. He had a flexion contracture of the wrist due to scar formation from an old forearm wound. Since this scar involved the skin and deeper tissue, it was thought that anything less than resection of the whole scar would not result in release of the contracture, therefore, resection of the scar with subsequent pedicle graft was advised. The day before operation the forearm was placed in a plaster of Paris cast and a large window cut over the proposed site of operation. Through the window, operation was performed, taking a pedicle from the abdomen. Position was maintained by extending a cast from the forearm around the body.

The postoperative course was uneventful. No inspection was made because the arm and body were encased in a cast. The second operation was performed fifteen days after the first, and the second postoperative course was uneventful. The flap took very well. Under physiotherapy the movement in the patient's fingers returned to 75 per cent. When the graft healed there was still some contracture of the fingers with the hand and wrist held at 180 degrees. A series of plaster casts was applied to the forearm and fingers, gradually stretching them to full extension by the end of two months (Fig. 5).

CASE 4.—F. D., a 58-year-old man, was admitted to the Cook County Hospital, April 19, 1938, because of an ulceration on the lower portion of the internal surface of the left foot. The examining room diagnosis was a squamous cell carcinoma at the base of the left toe. Casting and operation were performed, then a Thiersch split skin graft was applied to the area denuded by the pedicle. Vaseline gauze dressings were applied to both areas with moderate pressure of fluffed sponges over the pedicle graft. Both were immobilized in this position with a few rolls of plaster of Paris and held in position until set. The second stage operation was performed under general anesthesia. The pedicle skin graft flap from the right leg onto the medial side of the left leg was severed at the base of the flap; it was entirely viable and there were no areas of sloughing.

The patient was discharged on June 16. He returned to the clinic first at weekly intervals, later every two weeks. There was no recurrence of the ulceration and the deep tissues were healthy. Six months postoperatively there was little or no swelling and the part had assumed almost a normal appearance. The pathologic report was a squamous cell carcinoma ulceration. The condition of both the donor and defect sites was very satisfactory eighteen months after operation.

CASE 5.—E. H., a man aged 47 years, was admitted to the Cook County Hospital, June 28, 1938, with a chronic ulceration over the upper third of the left tibia on the anterior surface. He had a compound fracture of the left tibia in 1929, with infection of the bone and subsequent osteomyelitis. Six months later the bone was scraped. The donor site on the right leg was quite accessible and was covered with a Thiersch graft from the thigh area. The graft took and ultimately the entire area filled in from the edges.

localize in response to both chemical and bacterial irritants. It is interesting to note the similarity of the effect of adrenalin to narcosis on capillary permeability and inflammation in the skin of the rabbit.⁷

Adrenalin when given intradermally and intravenously in large quantities inhibits the development of hyperemia in areas of skin where xylol is applied. Trypan blue when given intravenously, fails to localize and to concentrate in areas of the rabbit's skin where adrenalin is injected intradermally and xylol is applied locally, although the areas become reddish brown in color after twenty to thirty minutes.

Capillary permeability and inflammation have been studied in rabbits with staphylococcal septicemia.⁷ It was noted that capillary permeability and inflammation, as observed in the skin, is different in a rabbit with a staphylococcal septicemia from that in a normal rabbit. This variation apparently may be the result of constriction of small cutaneous blood vessels. This reaction in the skin is similar to that which may occur in rabbits anesthetized with either alcohol or ether, or injected with large quantities of adrenalin.

An experimental study of capillary permeability and inflammation in rabbits with lowered blood pressure is considered important in view of the previous experiments and the subsequent observations to be reported on capillary permeability and inflammation in shock.

METHODS AND MATERIALS

In our experiments rabbits are used. The blood pressure is recorded from the carotid artery either by a mercury manometer or on a kymograph. The tissues in the neck are anesthetized with a 1.0 per cent solution of novocain. A 1.0 per cent solution of sodium citrate is used as the anticoagulant in washing the cannula and the tubing. The length of time during which the animals are observed in these experiments varies from an hour to six hours.

The arterial blood pressure is lowered either by removing blood through the cannula or by bleeding directly from the heart. Sometimes multiple small bleedings are made, while in other experiments a single large volume of blood is removed. The quantity of blood to be removed is determined by the level of the blood pressure.

The skin is shaven carefully twenty-four hours or longer before the experiment is begun. Xylol is applied carefully to local areas of skin at varying intervals before 10.0 to 15.0 c.c. of a 0.2 per cent solution of trypan blue is injected intravenously in those experiments where capillary permeability is studied. The time and the amount of dye that localizes in the different areas of skin is recorded.

Macroscopic and microscopic observations are made on the xylol-treated areas of the skin, the areas injected intradermally with a heavy saline suspension of staphylococci, and also with a 2.0 per cent suspension of alenronate. Sections of the skin are removed at different inter-

THE EFFECT OF LOW BLOOD PRESSURE UPON CAPILLARY PERMEABILITY AND INFLAMMATION IN THE SKIN OF RABBITS*

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ONE of us (R. H. R.) has been interested in the factors that influence capillary permeability and inflammation in the skin of the rabbit. The mechanism by which increases in capillary permeability may occur has been discussed frequently.¹⁻³ The localization and the concentration of certain colloidal dyes following intravenous injection has been used to demonstrate changes in capillary permeability. An increase in capillary permeability occurs when the dye localizes and concentrates more quickly in one area of skin than it does in another in the same animal.

Trypan blue injected intravenously localizes and concentrates in areas of inflammation produced by xylol in the rabbit.⁴ The time required for the localization of the dye and the quantity of dye that localizes and concentrates in an area of inflammation is influenced by the interval between the application of the irritant and the injection of the dye. The greatest quantity of dye localizes and concentrates in the area where xylol is applied the shortest time before the dye is given. There is a progressive diminution in the quantity of dye that concentrates in xylol-treated areas when the interval between the application of xylol and the injection of the dye is progressively increased. When xylol is applied three hours or longer before the dye is injected, essentially the same amount of dye localizes in the xylol-treated areas as in the untreated skin.⁴

Macroscopic and microscopic observations are made in the studies on inflammation and the presence or absence of leucocytes about the irritants is considered significant. The relationship of capillary permeability, as defined above, to the presence of polymorphonuclear leucocytes in areas of inflammation has been discussed.³

Capillary permeability and inflammation have been studied in narcotized rabbits.⁵ Capillary permeability in areas of inflammation is altered in rabbits narcotized with both alcohol and ether as demonstrated by the localization and the concentration of trypan blue. The inflammatory response may be either greatly diminished or only slightly decreased in rabbits narcotized with alcohol and ether, as indicated by the amount of hyperemia, edema, and the number of leucocytes that

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A reddish brown color similar to that observed in rabbit X-1 has been observed and described in other experiments.⁶

Rabbit X-22

- 4:20 P.M. Cannula put into carotid; blood pressure, 140.
- 4:25 P.M. 30 c.c. of blood removed from heart; blood pressure, 50. The skin over the entire body is pale.
- 4:30 P.M. Xylol applied to the skin in area 1.
- 4:34 P.M. There is no hyperemia of the skin in area 1.
- 4:35 P.M. Xylol applied to the skin in area 2.
- 4:40 P.M. Xylol applied to the skin in area 3.
- 4:42 P.M. No hyperemia or edema in any of the xylol-treated areas of the skin.
- 4:45 P.M. Blood pressure, 80.
- 4:50 P.M. Xylol applied to the skin in area 4; blood pressure, 88.
- 4:54 P.M. Xylol applied to the skin in area 5.
- 5:00 P.M. Xylol applied to the skin in area 6; 10 c.c. of trypan blue given intravenously.
- 5:15 P.M. There is no dye in any of the xylol-treated areas.

The pale appearance of the skin immediately following the withdrawal of blood would suggest constriction of the cutaneous vessels. The absence of the development of hyperemia and edema in the skin of this rabbit and the failure of trypan blue to localize within a period of fifteen minutes is certainly different from the reaction in the normal rabbit.

The following protocol illustrates the variation in the localization of trypan blue in rabbits with a lowered blood pressure as compared with the normal.

Rabbit X-2

- 3:15 P.M. Blood pressure, 120.
- 3:35 P.M. 20 c.c. blood removed through the cannula.
- 3:45 P.M. Blood pressure, 70.
- 3:50 P.M. Xylol applied to the skin in area 1.
- 4:00 P.M. Very little hyperemia is present in area 1.
- 4:15 P.M. Xylol applied to the skin in area 2; blood pressure, 74.
- 4:22 P.M. No hyperemia is present in area 2.
- 4:45 P.M. Xylol applied to the skin in area 3. The skin in areas 1 and 2 is a little reddish brown.
- 5:10 P.M. Xylol applied to the skin in area 4; blood pressure, 56.
- 5:15 P.M. Xylol applied to the skin in area 5.
- 5:18 P.M. Xylol applied to the skin in area 6; 10 c.c. of trypan blue given intravenously.
- 5:20 P.M. Blood pressure, 74.
- 5:25 P.M. A little dye is present in area 3.
- 5:27 P.M. A little dye is present in areas 2, 3, and 4.
- 5:40 P.M. The largest amount of dye is present in area 3. Approximately the same amount of dye is present in areas 2 and 4, less dye in area 5 than in area 4, and less in 6 than in 5. There are approximately a dozen small blue areas 1 to 2 mm. in diameter in area 1.
- 6:00 P.M. The quantity of dye is gradually increasing in areas 5 and 6. There is about the same amount of dye in areas 4 and 6, only a little in 2 and none in 1 except for the small pinpoint collections. There is no trypan blue in the untreated skin of this rabbit.

vals following the injection of the irritants. They are fixed in a 10 per cent solution of formalin. Paraffin sections are prepared and stained with hematoxylin and eosin.

OBSERVATIONS ON CAPILLARY PERMEABILITY IN THE SKIN OF RABBITS WITH A LOW BLOOD PRESSURE

Seventeen rabbits are used in this experiment. A majority of these are adult rabbits weighing from 1.5 to 3.0 kg. A few young rabbits are used.

It is difficult to standardize the experimental procedure since the degree of the fall in blood pressure varies so widely in the different rabbits. The following protocols are selected to illustrate the changes observed in the localization of trypan blue in adult rabbits:

Rabbit X-1

- 2:45 P.M. Cannula put into carotid; blood pressure, 144.
- 2:44 P.M. 40 c.c. of blood removed through cannula; blood pressure, 48.
- 3:05 P.M. Blood pressure, 128; 10 c.c. blood removed.
- 3:10 P.M. Xylol applied to the skin in area 1.
- 3:20 P.M. Xylol applied to the skin in area 2.
- 3:30 P.M. Xylol applied to the skin in area 3. The skin in area 1 has a reddish brown color.
- 3:30 P.M. Xylol applied to the skin in area 4; blood pressure, 98.
- 3:50 P.M. Xylol applied to the skin in area 5.
- 3:55 P.M. Xylol applied to the skin in area 6.
- 4:00 P.M. There is no hyperemia in areas 3, 4, 5, and 6. Xylol applied to the skin in area 7; 15 c.c. trypan blue given intravenously.
- 4:05 P.M. No dye has localized in any of the xylol-treated areas of the skin.
- 4:20 P.M. Areas 1 and 2 are reddish brown in color and there are small blue spots in the area. Trypan blue is present at the periphery of the xylol-treated skin.
- 4:25 P.M. A small amount of dye is present in areas 5 and 6.
- 4:40 P.M. There is a diminution in the intensity of the reddish brown color from area 1 to area 7. There is no dye in area 7.
- 4:45 P.M. Little spots of dye are present in areas 1, 2, 3, and 6.

In rabbits with normal blood pressure the dye usually appears in the last area of skin treated with xylol within a period of five minutes. In these rabbits with lowered blood pressure, the time required for the dye to localize is much longer and sometimes it fails to localize. The localization of the dye at the periphery instead of within the xylol-treated area has never been observed in the normal rabbit. Blue areas 1 to 2 mm. in diameter, in the xylol-treated areas, have not occurred in the rabbits with normal blood pressure. The dye localizes and concentrates in the skin in a uniform manner in the normal rabbits where xylol is applied.

Frequently there is no hyperemia after the application of xylol to the skin of rabbits with low blood pressure. Hyperemia occurs 15 to 30 seconds following the application of this irritant in normal animals. Edema rapidly follows the hyperemia and both remain for several days.

of rabbits with low blood pressure. Polymorphonuclear leucocytes may also fail to localize in the corium in such animals. Trypan blue injected intravenously may also fail to localize and to concentrate in the xylol-treated area of skin. All of these variations suggest that the small blood vessels constrict in the skin of rabbits following removal of blood and when in this state they fail to react to the local applica-



Fig 1.

A—Rabbit 336 Cannula put into carotid artery. B.P., 106 mm. Hg. 20 c.c. blood removed through cannula. B.P. 76 mm Hg. 0.2 c.c. of a saline suspension of staphylococci injected I.D. B.P. after 6 hours, 14 mm. Hg. Section of skin removed six hours after bacteria injected. Note the absence of leucocytes about the groups of bacteria. The pressure is recorded on a mercury manometer.

B—Rabbit 337 B.P. not taken. Injected the same as rabbit 336. Leucocytes are infiltrating the tissue around the clumps of bacteria.

tion of xylol. Furthermore, since they are constricted, trypan blue and polymorphonuclear leucocytes cannot reach the area of the irritants. It was thought that a vascular constriction of the small vessels in the skin occurred in rabbits given large amounts of adrenalin both intravenously and intradermally. Because of this constriction, hyper-

All rabbits do not show so great a variation in the time in which trypan blue localizes in the xylol-treated areas as compared with a normal adult animal. The following protocol illustrates the localization of trypan blue in xylol-treated areas of a normal rabbit.

Rabbit 5

- 1:55 P.M. Xylol applied to the skin in area 1.
- 2:10 P.M. Xylol applied to the skin in area 2.
- 2:25 P.M. Xylol applied to the skin in area 3.
- 2:40 P.M. Xylol applied to the skin in area 4.
- 2:45 P.M. The xylol-treated areas of skin are hyperemic and edematous.
- 2:53 P.M. Xylol applied to the skin in area 5.
- 3:10 P.M. Xylol applied to the skin in area 6; 10 c.c. of trypan blue given intravenously.
- 3:13 P.M. Dye is present in areas 5 and 6, the greatest amount being in area 6.
- 3:25 P.M. The greatest amount of dye is present in area 6, with a progressive decrease in the quantity in areas 6 to 1.

MACROSCOPIC AND MICROSCOPIC EVIDENCES OF INFLAMMATION IN RABBITS WITH LOW BLOOD PRESSURE

In the preceding experiments it was shown that the skin of rabbits with low blood pressure may fail to become hyperemic following the application of xylol. Twenty rabbits are used in this experiment to study the inflammatory reaction. The normal arterial pressure is determined in fourteen of the animals before bleeding and at varying intervals thereafter. Six of them are used as controls. All the rabbits are injected intradermally with a suspension of both staphylococci and aleuronat six hours, four hours, and two hours before they are killed. Xylol is also applied to other areas of skin at the same intervals.

There is a wide variation in the arterial pressure in these animals. However, there always appears to be a relationship between the arterial pressure and the macroscopic evidences of inflammation. When the pressure is around 60 mm. Hg there is a definite decrease in the amount of hyperemia and edema and a diminution in the number of leucocytes which localize in the tissue. These changes are nicely illustrated by rabbit 336 in which the decrease in the number of leucocytes is very conspicuous (Fig. 1A). The control for this animal shows a diffuse infiltration of the tissue with polymorphonuclears (Fig. 1B). Leucocytes may fail to localize about both staphylococci and particles of aleuronat when the blood pressure is lower than 50 mm. Hg. No macroscopic reaction occurs in the skin of rabbit 336 following the injections of the irritants and essentially no polymorphonuclear leucocytes are present in the histologic section.

DISCUSSION

The observations made in this study show that the reactions in the skin are different in a rabbit with low blood pressure from those of a normal rabbit. Xylol may fail to produce any hyperemia in the skin

bits to localize and to concentrate about the bacteria? Thirty cubic centimeters of blood are removed from each of four rabbits and white blood cell counts are made on the blood obtained from the ear of each rabbit at frequent intervals during a period of six hours. This quantity of blood is similar to that removed from other rabbits in these experiments. There is a slight increase in the number of white blood cells above the normal in each of these rabbits. This observation would suggest that the failure of leucocytes to localize about the bacteria may not be due to their complete absence in the circulating blood.

To determine the effect that a decrease in the number of leucocytes may have upon the development of any inflammatory reaction a group of four rabbits is given subcutaneous injections of benzene in olive oil. The white blood cell counts are followed daily and when the number of leucocytes reach 3,000 or less a saline suspension of staphylococci is injected intradermally. The macroscopic reaction in the skin appears to be identical with that in rabbits with a normal number of circulating leucocytes. These observations also appear to support the opinion that the failure of leucocytes to localize and to concentrate about staphylococci in rabbits with low blood pressure may be the result of vascular constriction in the small, cutaneous vessels and not the result of a diminution in the number of leucocytes in the circulation blood.

Low blood pressure in rabbits alters the reactions to irritants in the skin. There is a diminution in the degree of hyperemia and edema about the foci of injected staphylococci and aleuronat and a decrease in the number of polymorphonuclear leucocytes which localize in the tissue around these irritants. In rabbits with very low blood pressure both macroscopic and microscopic changes may fail completely to develop.

Trypan blue injected intravenously localizes in areas of inflammation in the skin of rabbits with low blood pressure in a different manner from what it does in normal rabbits. This dye may fail to localize in areas of inflammation in some of the rabbits with exceedingly low arterial pressures.

REFERENCES

1. Burrows, H.: *Some Factors in the Localization of Disease in the Body*, New York, 1932, William Wood & Company.
2. Menkin, V.: *Dynamics of Inflammation*, New York, 1940, The Macmillan Company.
3. Rigdon, R. H.: Relation of Capillary Permeability to Inflammation, *South. M. J.* 34: 292, 1941.
4. Rigdon, R. H.: Capillary Permeability in Areas of Inflammation Produced by Xylene, *Arch. Surg.* 41: 101, 1940.
5. Cressman, Ralph D., and Rigdon, R. H.: Capillary Permeability and Inflammation in Narcotized Rabbits, *Arch. Surg.* 39: 586, 1939.
6. Rigdon, R. H.: A Study of Capillary Permeability and Inflammation in the Skin of Rabbits Given Adrenalin, *Surgery* 8: 839, 1940.
7. Rigdon, R. H.: A Study of Capillary Permeability and Inflammation in the Skin of Rabbits With Staphylococcal Septicemia, *Arch. Surg.* 44: 129, 1942.

emia failed to occur and trypan blue did not localize following an intravenous injection.⁶

The variation in the time required for trypan blue to localize and to concentrate in xylol-treated areas of skin in rabbits with low blood pressure as compared with the controls is also interesting. If trypan blue localizes and concentrates in xylol-treated areas of skin as the result of a metabolic change in the cells, then the rate at which this change occurs is influenced by the acute loss of blood.³ The changes in the epithelial cells in the skin following the application of xylol are much slower in rabbits with low blood pressure. It must be remembered that each of these observations on the localization and concentration of trypan blue in xylol-treated areas of skin is made in the same rabbit.

The observations made in this experiment are more significant when it is recalled that trypan blue localizes and concentrates in one area of the skin and not in another when both are treated exactly alike. This variation results from the difference in the time that the xylol is applied to the areas and the dye is injected intravenously. The quantity of dye in the circulating blood progressively decreases following inoculation. This factor, however, apparently will not explain either the variations in the localizing of the dye in the different xylol-treated areas of skin in a normal rabbit or the variations observed in a rabbit with low blood pressure resulting from the withdrawal of blood.

Trypan blue injected intravenously localizes and concentrates in a normal rabbit more or less uniformly throughout the area of skin treated with xylol. In some of the rabbits with low blood pressure this dye localizes and concentrates at the periphery of these xylol-treated areas of skin. The reddish-brown color of the xylol-treated areas of skin which is usually present in such animals has been observed in other experiments.⁶ At this time we have no information or suggestions as to the mechanism of this phenomenon in which trypan blue localizes and concentrates at the periphery of a reddish-brown zone of xylol-treated skin and not in the center. Vascular occlusions have not been noted in the histologic sections. The rabbit's blood pressure must be very low before there is a significant decrease in the development of the inflammatory reaction as shown by the macroscopic changes in the skin and by the diminution or complete absence of leucocytes in the tissues. Variations in the localization and the concentration of trypan blue may be observed in animals with a pressure somewhat higher than that which is present when leucocytes fail to localize in the area of tissue about the irritants.

It is difficult to maintain the rabbits for several hours with very low blood pressures and many of them die. Clotting occurs in the cannula and makes recording unsatisfactory.

There is one important factor to consider in these studies. Is there a sufficient number of leucocytes in the peripheral blood of these rab-

cal procedure. Of the 179 patients having removal of the tumor, the hospital mortality rate was 7.2 per cent. The operations performed were one-stage abdominoperineal resections of the rectum in 129 patients with 10 per cent hospital mortality, 28 two-stage Mummery operations, 16 two-stage obstruction resection operations, and when the tumor was at the rectosigmoid junction 5 local removals of small tumors and one resection of the retroperitoneal rectum, all the latter groups with no mortality. During the past ten years we have become increasingly convinced that the one-stage abdominoperineal operation is the operation of choice in most patients. For instance, since 1935 we have done a one-stage abdominoperineal operation 114 times to 5 two-stage Mummery operations during the same period.

A report on the ultimate survival of the patients will be the subject of another communication but our impression is that the extension of operative indications to include cases of doubtful operability is fully justified by the survival rate.

In 93 (34 per cent) patients of the 272 operated upon, the growth was considered inoperable for the following principal reasons:

Extensive liver metastases	40
Infiltration of the growth into the base of the bladder	28
Marked infiltration of the growth into the prostate, vagina or sacrum	25

Table I gives all the causes of inoperability in 98 patients.

TABLE I

CAUSES OF INOPERABILITY IN 98 PATIENTS OF 277 OPERATED UPON

1. Extensive liver metastases	40
2. Infiltration of the tumor into the base of the bladder	28
3. Marked infiltration of the tumor into the prostate, vagina, or sacrum.	25
4. Perforation of the tumor into the soft parts	3
5. Eighty or more years of age and bronchitis or bronchiectasis	1
6. Extensive peritoneal involvement	2
7. Attachment to the posterior abdominal wall	1
8. Large glands along the aorta	1
Total (one patient had more than one cause)	99

Colostomy was performed in 89 of these inoperable patients, with an operative mortality of two (2.3 per cent). The incision was closed in nine patients without doing anything because it was felt that death would ensue before obstruction of the bowel from the tumor would occur. These patients had extensive involvement of the liver, and small tumors causing few symptoms.

We have considered definite liver involvement with metastatic cancer as a contraindication to radical removal of the primary growth in the rectum. There were forty patients or 42 per cent of the whole inoperable group in this category. When, however, one or two small nodules were palpated in the liver, the liver was sandy, or there was any doubt

A CONSIDERATION OF THE CONTRAINDICATIONS FOR RADICAL OPERATION IN CANCER OF THE RECTUM

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DUE to the radioresistance of carcinoma of the rectum, it is generally agreed that radical operative removal of the tumor offers the best chance of cure. It therefore follows that the higher the operability rate the greater will be the number of patients given a chance of cure. The factors entering into the determination of the operability rate assume great importance in the mortality rate of the operation as well as in the ultimate survival of the patients operated upon. The operability rate depends primarily on the experience of the surgeon in that his judgment must determine whether the growth can be entirely removed with a reasonable mortality and survival rate. As the operability rate rises, the technical difficulties of the operation increase. The operative mortality rises but the *total* number of patients given several years of health or permanent cure should increase. There consequently is a dividing line where in the opinion of the operating surgeon the growth cannot be removed or the patient could not survive the operation.

It is the purpose of this paper to review our personal experience in the last ten years of the operative treatment of cancer of the rectum as it concerns the contraindications for radical removal of the growth. The group of patients concerned are those entering the hospital for operation, and exclude those seen in consultation. This formula is adopted because many patients were seen in consultation, whom we considered operable or inoperable, who either refused operation or went elsewhere.

In reviewing our material from 1930 to August, 1941 we found that we had admitted to the Presbyterian Hospital, for operation, 277 cases of carcinoma of the rectum. Of these we considered five inoperable, one due to vaginal metastases and four because of firm fixation to the sacrum and prostate. The remaining 272 patients were operated upon. Of these remaining 272 cases, 179 were radically operated upon (66 per cent). Of these 179 having removal of the tumor, 105, or 55 per cent, were doubtfully operable due to age (38 over 65 years of age); one or two doubtful nodules in the liver, 15; dense pelvic adhesions, 9; obesity, 10; necessity of resection of the bladder, ureter, prostate, rectovaginal septum, urethra, or adnexa, 18, with the tumor, as well as to other factors not so easily classifiable.

In view of the extension of the indications for radical operation it is obvious that the mortality rate should be kept within a reasonable figure and that the long survival rate after operation should justify the radi-

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There were 23 cases deemed inoperable because of advanced infiltration and fixation of the tumor to the prostate, sacrum, or rectovaginal septum. As already indicated, 5 of these patients were not operated upon at all due to the short life expectancy and most of the others were given a colostomy because of approaching obstruction and marked infection of the tumor. These patients lived on an average of eleven months after operation and were a most distressing group, requiring increasing doses of sedatives. The border line between inoperable fixation and operability where a large part of the prostate or rectovaginal septum is removed with the tumor is not easy to define. We have increased gradually the indications for operation in that group and in the period under discussion have removed a part of the prostate, urethra, or rectovaginal septum in thirteen patients. There were two postoperative deaths but otherwise we are in favor of the procedure. We have also removed a part of the sacrum in a few patients but we have not felt encouraged to continue doing so.

Perforation of the tumor into the soft parts or with abscess formation was a contraindication for operation in three patients. This complication is not a frequent one and is not an absolute bar to radical removal of the tumor if it is possible to include the soft parts in the resected specimen.

Two patients had rather extensive peritoneal involvement with carcinoma, which made radical operation inadvisable but the presence of peritoneal plaques of carcinoma around the intraperitoneal tumor has not deterred us from radical operation. The prognosis in that group will, of course, be considerably clouded.

During this period we have considered age alone as contraindication for radical operation in only one patient, a man 81 years of age with a marked bronchitis. Thirty-eight patients over 65 years of age have had surgical removal of their tumor and while the operative mortality (four deaths) from pneumonia and embolism is higher in this group than in a younger age group, the survival rate justifies the procedure. The type of operation used in this age group must be selected carefully.

The size of the tumor has relatively little to do with its operability. Small tumors may have extensive metastases into the glands or liver and large tumors may have none. The only disturbing factor in large tumors is the mechanical one and we favor the one-stage abdominoperineal operation exclusively in that group.

Enlargement of the lymphatic glands along the superior hemorrhoidal and inferior mesenteric vessels or even along the aorta is not considered a contraindication to operation because many such glandular enlargements are due to infection and we have found from a careful study of these glands that it is not possible to be sure of the nature of the enlargement without histologic examination. Where glands are grossly enlarged it is wise to extend the upper limits of the operation as far

as to the character of the nodules in the liver, radical operation was carried out. This principle is particularly important because the differential diagnosis between angiomas or adenomas of the liver and early carcinomatous lesions is extremely difficult to make and especially so when the only method available is the sense of touch. We are aware of the fact that several experienced surgeons have advocated radical removal of the cancerous rectum when definite but early involvement of the liver was present. In view of the tedious convalescence following radical removal of the rectum and the short life expectancy (ten months in our cases) where definite liver involvement is found at the operation, we have not considered such a course a sound one. On the other hand, colostomy has been omitted in a number of patients with advanced cancer of the liver and a small rectal growth where it was felt that death from the liver involvement would occur before obstruction took place. Some of these patients have died of intercurrent disease without becoming aware of the hopelessness of their condition. Naturally, this latter group is a small one and is mentioned only to emphasize the importance of individualization in the cases of this inoperable group.

The second largest cause of inoperability is infiltration of the tumor into the base of the bladder. There were 28 cases, or 29 per cent of the whole inoperable group, in this class. This is a very distressing group due not only to their inevitable suffering from a progressive infiltration and often a final rupture into the bladder but also to their tendency to live on an average of fifteen months after the exploratory operation. In the earlier cases we used radium treatment by inserting radium into the growth from the rectal side or by the additional use of radium packs. There is no question that the rate of growth of the tumor is lessened but there is also but little doubt that the patients' suffering is increased. One patient given very extensive radiation lived for three years but it hardly seemed worthwhile in view of the suffering entailed. No patient was cured by radium and it seemed very probable that perforation into the bladder was hastened in some.

In contrast to infiltration of the dome or posterior surface of the bladder where resection of the bladder with the tumor is always carried out, we have adopted a rather hopeless view in the cases having infiltration of the base of the bladder and have not attempted resection. This may be an incorrect decision, particularly in otherwise favorable risks, and perhaps attempts should be made in a small series of cases to resect the base of the bladder and transplant the ureters into the dome of the bladder. Reckless surgery is bad surgery but in this group we are faced with 100 per cent mortality, with a relatively long life expectancy if no attempt at removal is made. It is therefore reasonable to consider the possibility of extension of the indications for radical operation in a small group of otherwise favorable risks.

Editorial

Contamination of the Peritoneum

CONCURRENT with widening possibilities in the prevention and control of surgical infections through recent developments in chemotherapy, the distinction between contamination and infection of wounds is receiving the attention it deserves. Curiously enough, few observers have made the same distinction in regard to the peritoneum in association with disease, particularly appendicitis. That the distinction is valid in the peritoneum, as elsewhere, is indicated by established surgical principles under conditions in which the contaminating organisms are less virulent and less numerous than in appendicitis, as in perforation of a duodenal ulcer. It is widely recognized that the peritoneum, although contaminated, may escape infection if the source of contamination is promptly eliminated. During operation on a perforated duodenal ulcer one often sees gross changes which are compatible with peritonitis, that is, injection, dulling, fibrin deposits, and free fluid, even a short time after the contamination has occurred. That these appearances are not necessarily evidences of established peritoneal infection is quite clear from the subsequent course of the disease. What they represent, in fact, is an inflammatory process in response to contamination and chemical damage, resulting in destruction of invading organisms. The histologic picture of a contaminated wound which is successfully handling contamination differs from the histologic appearance of this inflammatory process in the peritoneum only through the differing natures of the tissues involved.

It is quite obvious that mere inspection of, or even positive culture from, the peritoneal surfaces, after contamination from a perforated duodenal ulcer, does not indicate whether or not a definitely established infection of the peritoneum will eventuate. The same is true of the appearances in the neighborhood of a recently perforated appendix. Yet almost all authors classify as peritonitis any perforation of the appendix which shows an inflammatory process in the neighboring peritoneum. As was pointed out by Lehman and Parker,¹ among others, many of these early perforations are no more than contaminations of the peritoneum and do not present the real problems of an established peritonitis if the source of the contamination is promptly removed. Just as in accidental wounds, only the subsequent course of the disease will indicate whether or not peritonitis has occurred.

as possible, ligating the superior mesenteric artery just distal to the first sigmoid branch and in some instances carrying dissection of the soft parts above the ligation.

Attachment of the intraperitoneal portion of the tumor to the uterus or adnexa, dome of the bladder, ureter or other loops of bowel should not be a contraindication to radical operation as these structures can be removed with the tumor.

Adiposity is no contraindication per se for radical operation although it must be said that the technical difficulties of the operation are increased from the standpoint of exposure and control of hemorrhage and that postoperative complications such as disruption of the wound, infection of the wound, and cardiovascular unbalance are more to be anticipated. One patient died postoperatively in this group but no patient was refused operation because of adiposity.

Diabetes, cardiovascular disease, anemia, avitaminosis, low serum protein, dehydration, and partial obstruction of the bowel are all treated medically in the preparatory stage admitting all cases a week before the operation. If the obstruction of the bowel cannot be taken care of medically by diet, large enemas, and mild saline laxatives, a preliminary colostomy is done. This is necessary in a relatively small number of cases.

SUMMARY

Of 277 patients coming to the hospital for operation for cancer of the rectum, 98 were considered inoperable. Of these, 84 were colostomized.

The contraindications for removal of the tumor were liver metastases in 40, attachment to the base of the bladder in 28, and infiltrative attachment to the sacrum, prostate, or rectovaginal septum in 23.

Adiposity, age, cardiovascular disease, large tumors, enlargement of regional lymph glands, resectable attachment of the tumor to the prostate, rectovaginal septum, uterus, or adnexa, dome of the bladder or ureter are not considered contraindications to radical removal of the tumor.

The decision to extend the indications for radical operation in cancer of the rectum so that 65 per cent of the patients coming to the hospital for operation may be given the benefit of curative operation will increase the operative mortality but will result in an actually larger number of patients being given a long-term cure.

all. Certainly most of them would have had an equally smooth course without the use of the drug.

Such comments are not meant to imply any disapproval of the local use of the sulfonamides in cases of contamination of the peritoneum. According to our present knowledge of their effectiveness it is probable that in these cases their use is most justified and presents the best promise of utility.

The real problem is to obtain a true statistical picture of the results of the treatment of true peritonitis, a highly fatal disease, the control of which is far from satisfactory with or without chemotherapy. There is no possibility of judging how effective the sulfonamides or any other treatment may be in true peritonitis so long as cases of contaminated peritoneum are permitted to fog the results. It is urged that the distinction between contamination and infection, now so well established in surgical thought in dealing with other tissues, be kept in mind when dealing with the peritoneum in connection with appendicitis. An inflammatory process of the peritoneum representing the defense mechanism against contamination is by no means, necessarily, in practical effect an established peritonitis with the difficult clinical problems presented by that disease.

REFERENCES

1. Lehman, E. P., and Parker, W. H.: The Treatment of Intraperitoneal Abscess Arising From Appendicitis, *Ann. Surg.* 108: 833-856, 1938.
2. Penberthy, Grover C.: Appendicitis in Infants and Children; a Fifteen-Year Review; read before the American Surgical Association, Cleveland, April 8, 1942.
3. Tashiro, K., Pratt, O. B., Kobayashi, N., and Kawaichi, G. K.: The Local Implantation of Sulfanilamide in the Peritoneal Cavity, *SURGERY* 11: 671-689, 1942.

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The unmistakable fact of perforation of the appendix has too long governed the classification of the complications of appendicitis. Although contamination of the peritoneum must obviously precede infection, yet it does not necessarily establish the occurrence of the more serious complication.

Any statistical study which groups all perforations of the appendix under the head of Peritonitis is presenting a distorted picture of the latter. The effect of this type of classification is to improve tremendously the mortality rate of peritonitis inasmuch as that group then contains a large percentage of cases which have actually never been true peritonitis. The cases of contaminated peritoneum can justly be included, after the postoperative course is known, in the group of uncomplicated appendicitis, as was done by Lehman and Parker. Inasmuch as, by definition, all these cases recover (with the exception of rare deaths from complications unrelated to the intra-abdominal disease) this procedure does not alter the mortality rate for the simple group. On the other hand, by excluding the contaminated peritoneum, it definitely presents a more accurate picture of true peritonitis. A second method of handling this group is one illustrated by Penberthy's recent paper,² in which, however, he still uses the term peritonitis. In his group of "acute unruptured appendicitis" the mortality is .44 per cent. It is noteworthy that the mortality of the group of "acute ruptured local peritonitis" is approximately the same as that of simple appendicitis, namely .55 per cent. This clearly indicates that this latter group is not peritonitis but presents only the contaminated peritoneum. Lehman and Parker in a series of cases of all ages reported a high mortality, namely 40.6 per cent, in their group of true peritonitis, whereas Penberthy's mortality in infants and children was as high as 64.9 per cent. (In both series localized peritonitis represented by an inflammatory mass or an abscess was properly reported as a separate problem.) These mortality figures for peritonitis are probably more nearly the correct figures than are those coming from clinics in which the number of cases of true peritonitis is diluted by a large percentage of cases of contaminated peritoneum. This effect is illustrated by combining Penberthy's groups of "acute ruptured local peritonitis" and "acute ruptured diffuse peritonitis," a procedure that results in a mortality of 22.3 per cent for peritonitis from perforated appendicitis. Such a figure more nearly approaches the usual mortality reported.

The importance of this distinction in relation to appendicitis is emphasized at the present time by a large number of reports dealing with sulfonamide treatment of peritonitis. Tashiro, Pratt, Kobayashi, and Kawaichi³ report twenty-three cases of peritonitis from acute appendicitis treated by sulfanilamide intraperitoneally. Of these twenty-three cases, nine were operated upon within twenty-four hours of onset. These nine cases, nearly one-half, are not necessarily cases of peritonitis at

all. Certainly most of them would have had an equally smooth course without the use of the drug.

Such comments are not meant to imply any disapproval of the local use of the sulfonamides in cases of contamination of the peritoneum. According to our present knowledge of their effectiveness it is probable that in these cases their use is most justified and presents the best promise of utility.

The real problem is to obtain a true statistical picture of the results of the treatment of true peritonitis, a highly fatal disease, the control of which is far from satisfactory with or without chemotherapy. There is no possibility of judging how effective the sulfonamides or any other treatment may be in true peritonitis so long as cases of contaminated peritoneum are permitted to fog the results. It is urged that the distinction between contamination and infection, now so well established in surgical thought in dealing with other tissues, be kept in mind when dealing with the peritoneum in connection with appendicitis. An inflammatory process of the peritoneum representing the defense mechanism against contamination is by no means, necessarily, in practical effect an established peritonitis with the difficult clinical problems presented by that disease.

REFERENCES

1. Lehman, E. P., and Parker, W. H.: The Treatment of Intraperitoneal Abscess Arising From Appendicitis, *Ann. Surg.* 108: 833-856, 1938.
2. Penberthy, Grover C.: Appendicitis in Infants and Children; a Fifteen-Year Review; read before the American Surgical Association, Cleveland, April 8, 1942.
3. Tashiro, K., Pratt, O. B., Kobayashi, N., and Kawaichi, G. K.: The Local Implantation of Sulfanilamide in the Peritoneal Cavity, *SURGERY* 11: 671-689, 1942.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

MENINGOCEREBRAL ADHESIONS

AN EXPERIMENTAL STUDY OF THE EFFECT OF HUMAN AMNIOTIC MEMBRANE, AMNIOPLASTIN, BEEF ALLANTOIC MEMBRANE, CARGILE MEMBRANE, TANTALUM FOIL, AND POLYVINYL ALCOHOL FILMS

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INTRODUCTION

IN THE World War of 1914-1918 the treatment of craniocerebral injuries was steadily improved. The passage of each year brought the adoption of new surgical principles directed not only toward the lowering of the mortality rate but, in addition, the prevention of early and late complications. Many of these early deaths were on the basis of infection, a complication which will be largely overcome in the present emergency by the judicious use of chemotherapy. The late complications have been the problems of the postwar years, namely, paralytic phenomena, disorders of speech, mental disturbances and post-traumatic epilepsy. This study was undertaken with a view to the better management of this last-named complication.

Penfield^{51, 53, 54} has repeatedly emphasized the importance of the meningeal ingrowth of the cerebral wound in the production of convulsive phenomena. In contradistinction to the past theories which stressed the importance of the mechanical pull on the brain alone, he believes that the responsible element in rendering the scar epileptogenic is the establishment of a crossed circulation with the overlying tissues. This leads ultimately to destruction and revascularization of the cerebral cortex. In 1930, he collaborated with Foerster²² in a study of twelve cases of post-traumatic epilepsy. In a few of these patients seizures were induced on the operating table by tugging on the dura overlying a meningocerebral cicatrix. On the basis of these observations they suggested that a vasomotor reflex secondary to traction may be responsible for the initiation of seizures.

As further evidence for the importance of meningeal ingrowth, Penfield⁵¹ has pointed out the higher incidence of convulsive seizures following head injuries with, as compared to those without, dural penetration. Rawling⁵⁶ analyzed 452 cases of head injury sustained in World

War I and found the incidence of seizures following craniocerebral wounds of various types to be as follows: penetrating wound with hernia, 54 per cent; penetrating wound, 35 per cent; penetrating wound with foreign bodies retained, 33 per cent; perforating wound, 16 per cent; fractured base, 14 per cent; nonpenetrating wound, 13 per cent; scalp wounds, 10 per cent.

Wagstaffe,⁷⁰ in a study of 377 cases of gunshot wound of the head, noted a seizure incidence of 18.7 per cent in wounds with dural penetration and less than 2 per cent in those cases where the dura was not penetrated. The statistics of Stern, quoted by Schou,⁶⁷ are 20 to 50 per cent for open craniocerebral injury and 2 to 4 per cent for closed injury.

These observations, however, are not acceptable as evidence in favor of the importance of meningocerebral adhesions alone in the causation of seizures. Although the formation of adhesions would be greater in the cases with dural penetration, the destruction of nervous tissue would also be greater under these circumstances. Furthermore, it is likely that many of the nonpenetrating injuries were confined to the superficial structures and did not involve the underlying brain.

A third point of evidence in favor of the importance of meningeal ingrowth is Penfield's⁷¹ observation of the greater frequency of seizures in meningocerebral, as compared to cerebral, cicatrix. He believes that the incidence must be much lower in the cerebral cicatrix where there is little or no admixture of connective tissue. In support of this contention he points out the infrequency of seizures in patients with cerebral scars resulting from vascular occlusion.

This study is based on the theory that meningeal invasion is an important factor in determining the epileptogenic nature of a cerebral wound. The importance of the work is modified, therefore, by the acceptance or rejection of the adhesion hypothesis. However, this hypothesis will not be established as factual until a proved method of adhesion prevention is used in the surgical treatment of craniocerebral wounds and is followed in later years by a study of the incidence of post-traumatic epilepsy in cases so treated.

Our study is principally a continuation of the work of Chao, Humphreys, and Penfield¹² on the prevention of meningocerebral adhesions with amnioplastin, a membrane prepared from the human amnion. In addition, other materials including Cargile membrane, allantonic (insultonic) membrane, films of polyvinyl alcohol, and tantalum foil have been tried. Although an ideal material has not been found, the study has disclosed certain facts which must be considered in the use of these substances and, more important, in the final solution of the problem.

REVIEW OF THE LITERATURE

The problems involved in the prevention of meningocerebral adhesions have been approached in two directions, by reviewing (1) the factors

involved in the evolution of the meningocerebral scar, and (2) the methods which have been used in the past for this purpose.

The Formation of the Meningocerebral Cicatrix

Adherence to overlying structures is not the invariable component of cerebral injury. Any lesion, whether of a vascular, inflammatory or traumatic nature, which does not disturb continuity of the arachnoid, is not followed by adhesions. Our knowledge of this protective role of the arachnoid is due to the investigations of Harvey and his associates.

In 1923, Sayad and Harvey⁶⁴ published their observations on the reactions of the meninges to injury. They performed the first series of experiments on dogs. Discs of dura mater were excised leaving the leptomeninges uninjured. The dural defect was rapidly obliterated with blood clot, having only fibrinous attachments to the arachnoid. Within one week the arachnoidal surface of the clot was carpeted with a thin layer of endothelial cells and the fibrinous attachment to the arachnoid disappeared. They therefore concluded that the dura mater will regenerate without adhering to the intact arachnoid.

In the following year Lear and Harvey³³ reported their studies on the regeneration of the injured pia-arachnoid of dogs. To ensure the intactness of the overlying dura they reflected it from the cortical surface in the form of a large flap. The leptomeninges lying directly beneath the center of the dural flap were injured with either a blunt instrument or the electrocautery. Dural adhesions occurred in all instances. This led them to postulate that, in the repair of the leptomeninges, the dura mater does not serve as a limiting membrane but enters actively into the healing process.

The studies of Penfield^{49, 50} and Rio-Hortega and Penfield⁶⁰ have been valuable contributions to the pathogenesis of the meningocerebral cicatrix. They studied the sequence of events from within a few hours of the injury to the formation of the mature scar.

Within six hours of the injury the traumatic defect in the brain is filled with blood clot. The intensity of the fibroblastic-glial reaction which then ensues is directly proportional to the amount of remaining devitalized cerebral tissue. Within twenty-four hours the neighboring microglia develop an ameboid form and start their migration toward the site of injury. At the end of the second day they are compound granular corpuscles and are actively phagocytizing debris. This phagocytosis continues until all of the unnecessary materials have been removed. It is not uncommon to find these cells, filled with products of destruction, within the interstices of the scar many years after the injury. Penfield⁵³ describes one case in which fat-filled phagocytes were found in the border of a twenty-eight-year-old scar.

The astrocytes also play an important role in the repair process. At the end of the first day the astrocytes in the immediate neighborhood of

the wound have undergone elasmotodendrosis. Those in the more distant zone show swelling, without fragmentation, of both cell body and processes. On the fourth day these swollen cells undergo amitotic division and begin to lay down fibrils at the margin of the wound. By this time fibroblasts from the overlying dura muscle, and blood vessels have permeated the clot and are soon intimately blended with the neuroglia fibrils of the wound edge. Blood vessels proliferate and penetrate the fibroblastic-glial meshwork and eventually form a rich anastomosis with the cerebral vessels.

The final stage is one of contraction of the connective tissue core. This pull is transmitted to the glial fibrils causing them to be orientated perpendicularly to the surface of the cerebral wound. At times this traction is so great that the sucker feet of astrocytes are displaced through the pia mater. A further indication of the pull is the migration of the lateral ventricle toward the site of the lesion.

In summary, therefore, there are two factors which influence the formation of the meningeocerebral cicatrix. Most important is the damage to the arachnoid which predisposes the connective tissue invasion from the overlying structures. The second factor is the extent of brain destruction, the density of the resulting scar being directly proportional to the volume of devitalized tissue.

The Prevention of Meningocerebral Adhesions

The observations on methods and materials employed to prevent adhesions between the wounded brain and its enveloping structures are but few when compared to the voluminous literature on adhesion prevention in the other serous spaces of the organism. Especially impressive is the array of methods and materials used to prevent postoperative peritoneal adhesions. These are listed and discussed in the extensive reviews of Richardson⁵⁹ and Ochsner and Garside.⁴⁷ The size of this list is testimony to the difficulties presented in the solution of the problem. Similar difficulties exist in the prevention of adhesions in joint spaces and around sutured nerves and tendons.

In past years more attention has been focused on methods for the repair of dural defects than on the prevention of meningeocerebral adhesions. The materials and techniques for duraplasty have been reviewed by von Saar,⁶⁰ Bunné,⁶ de Bernardis,¹⁵ Caporale and de Bernardis,¹¹ and Glaser and Thienes.²⁵ These experiments have been of great interest and value in the present study. The reaction of the surrounding tissues to these materials, especially when the arachnoidal barrier is broken, has served as a guide in the selection of materials for this investigation. For purposes of review and discussion the materials used in the past for either duraplasty or the prevention of meningeocerebral adhesions may be classified as (1) metals, (2) viable animal membranes, (3) nonviable animal membranes, (4) miscellaneous materials.

Metals.—The debut of the modern period in the surgery of post-traumatic epilepsy, which was pioneered by Horsley in the latter part of the nineteenth century, was followed by the first reports on the use of materials to prevent meningocerebral adhesions. Horsley excised the epileptogenic cicatrices but did not cover the area of removal with protective materials. Beach is credited with the first suggestion to use these substances. In 1890, he³ described a case of post-traumatic epilepsy treated by lysis of the meningocerebral adhesions. At this time he stated that should the seizures recur he would reoperate and implant gold foil between the brain and dura. In 1897, he⁴ reported that this plan was effected at a secondary craniotomy in 1892. The patient's attacks recurred, but with diminished frequency and intensity. The condition of the foil was not mentioned.

The popularity of the metallic foils in the surgery of epilepsy was maintained well into the first decade of the twentieth century. The observations of Beach on gold foil were followed by the reports of Oliver,⁴⁸ Estes,¹⁹ Summers,⁶⁸ and Woolsey⁷¹ on this metal, those of Ray,⁵⁷ Harris,²⁹ and Prime⁵⁵ on silver foil, and Morehead,⁴⁴ and McCosh^{42, 43} on platinum foil. Chao, Humphreys, and Penfield¹² have recently reported their experiences with silver foil, aluminum foil, nickel plate, and stainless steel plate.

One feature common to all of these metals is encapsulation. The thickness of the capsule and the intensity of the cellular reaction have been variable. Both would seem dependent on the extent and character of the corrosion of the metal. The good clinical results obtained in some cases are overshadowed by the finding of dense adhesions between the brain and dura in all instances where direct observations on the condition of the metals were made.

Viable Animal Membranes.—At the close of the first decade of the twentieth century the metallic substances were being discarded in favor of viable and nonviable animal membranes. The viable membranes have generally been employed for the closure of dural defects and not for the prevention of meningocerebral adhesions. This work originated in 1909 when Kirschner^{34, 35} used autoplasmic fascia lata for dural restoration in dogs. The first human duraplastic operation with fascia lata was performed by Körte,³⁶ in 1910. A variety of viable membranes have since been employed. Among the autoplasmic tissues are dura,⁵ periosteum,^{6, 63} and fat.^{12, 16, 58} Homoplastic hernia sac was successfully used in man by Finsterer.^{20, 21} Burger⁸ attempted to replace the dura mater in cats with fresh, human amniotic membrane obtained at cesarean section but his results were inconclusive. Chao, Humphreys, and Penfield¹² present the only experimental data on the specific use of viable membranes to prevent meningocerebral adhesions. Both fat and fascia lata were used over brain wounds in cats. Adhesions occurred in all of the experiments.

An analysis of the results obtained by these observers allows certain conclusions to be drawn. From the standpoint of dural repair the autoplasmic, viable membranes have been uniformly successful. However, if the cerebral cortex was damaged meningeocerebral adhesions occurred.

Nonviable Animal Membranes.—A large number of materials classifiable in this category have been employed over the intact and damaged cerebral cortex. In 1898, Freeman²² described two experiments, one on a dog and the other on a rabbit, in which the vitelline membrane of the hen's egg was placed over the wounded brain. The experiment on the dog was inconclusive due to suppuration of the wound. At the end of two months the brain of the rabbit was yellow at the site of the wound but was smooth and nonadherent except by a few trivial and delicate adhesions around the edge of the dural opening. Greer²⁶ and Prime⁵³ subsequently reported their observations on this membrane. Prime noted adhesions in every instance if the cortex was damaged.

Other nonviable animal membranes which have been investigated are Cargile membrane,^{12, 13, 17} prepared hernia sac,^{20, 21, 69} human amniotic membrane,¹² heef allantoic membrane,¹² catgut membrane,^{11, 12, 15} sheep peritoneum,²⁷ and calf artery.⁶¹

These nonviable membranes have shown the greatest promise in the prevention of meningeocerebral adhesions. This is especially true of amniotic and allantoic membranes. While both materials provoke a foreign body reaction and are eventually encapsulated, the reaction has been comparatively minimal. Adhesions have been trivial or absent in a large number of the experiments. Caporale and de Bernardis¹¹ describe excellent results with catgut membrane. In their experiments on rabbits the membrane was adherent to the brain wound but not to the overlying structures. However, their good results were not confirmed in the experiments of Chao and his colleagues.¹²

Miscellaneous Membranes—Various substances of plant or mineral origin are included in this group, namely celluloid,²⁸ parchment,⁴⁶ mica and cellophane,¹² olive oil,⁷ and rubber tissue.¹ The experience with these materials has been generally unsatisfactory. With but few exceptions dense encapsulation and adhesion formation have been found at a later date.

THE SELECTION OF MATERIALS

An analysis of the results obtained with the aforementioned materials has been invaluable in the selection of substances for the present study. We have subjected a few of the more promising materials to further investigation. Other materials have been selected on the basis of the following characteristics.

1. Inertness. Provocation of minimal reaction in the surrounding tissues. This is the most important requirement.

2. Delayed resorption. The material should remain intact and check the ingrowth of fibrous tissue from the overlying structures throughout the period required for complete bridging of the cerebral wound by the arachnoid.

3. Availability of supply.

4. Ease of sterilization.

While an ideal membrane should possess all of these qualities, resorption would be dispensable if the material remained permanently inert in the tissues.

The materials used in this investigation may be classified as both resorbable and nonresorbable. They include, (1) amniotic membrane, in fresh, attenuated and fixed (amnioplastin) forms; (2) allantoic (insultic) membrane; (3) Cargile membrane; (4) tantalum foil; (5) polymerized vinyl alcohol films.

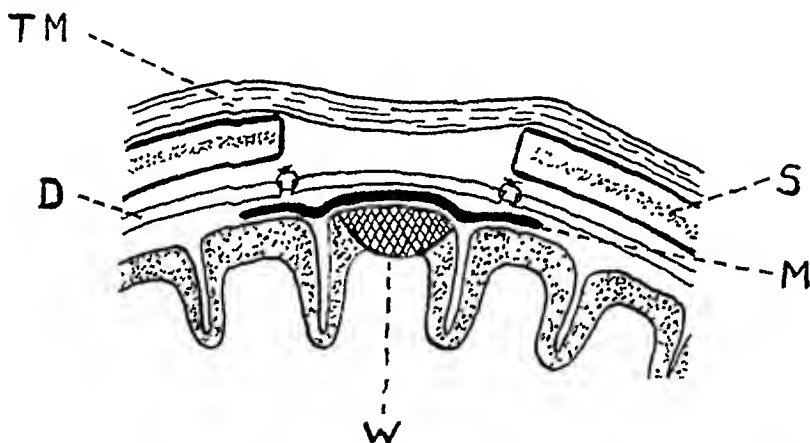


Fig 1—Diagrammatic cross section showing the method of covering the cerebral wound (W) with the membrane (M). Temporal muscle (T M), dura (D), skull (S).

EXPERIMENTAL DATA

A total of seventy-six cats was used during this study. All operations were carried out under rigid aseptic precautions. Bilateral openings in the skull, 15 to 20 cm. in diameter, were made in the parietal regions. The dura was incised about 2 mm. from the anterior, medial, and posterior margins of the bony defect and reflected laterally in the form of a flap. Wounding of the cerebral cortex was accomplished by electrocoagulation of the surface of one or more gyri. The area of thermal destruction was then pierced several times with the point of a scalpel. In some instances only one side of the brain was wounded. Both the wounded and unwounded cerebral hemispheres were covered with the material of choice and the borders were tucked well under the cut edges of the overlying dura (Fig. 1). The dura was closed with two

fine silk sutures. The temporal muscles, galea and skin were apposed with interrupted sutures of black silk.

The animals were killed at appropriate intervals varying from 4 to 240 days. Painstaking care was exercised in the removal of the brains. Prior to removal they were fixed in situ by the injection of 10 per cent formalin into both internal carotid arteries. The removed brain, well covered with dura over both the base and convexity, was placed in 10 per cent formalin until ready for gross section. When properly fixed it was sectioned in the coronal plane. One section was designed to pass through the center of the cerebral wounds (Fig. 2). The posterior block resulting from this section was examined grossly for adhesions. The anterior block was embedded in paraffin for microscopic study. To avoid distortion of the tissue relationships during the washing, dehydrating, clearing, and paraffin embedding processes, the dura was fastened to the brain and leptomeninges with black silk sutures. Sections for the histologic study were cut at a thickness 8 to 10 μ and stained with the hematoxylin and van Gieson, the Mallory phosphotungstic acid hematoxylin and the Mallory aniline blue methods.



Fig. 2.—Coronal section of the brain showing the wounds (W) in both cerebral hemispheres; the dura (D) is intact over the convexity and base.

Amniotic Membrane

Historical Survey.—In 1911, Schmerz⁶⁵ published a report of the first known attempt to use amniotic membrane for the prevention of adhesions between serous surfaces. He used a formalinized human amniotic membrane with success in the treatment of disabling adhesions in three patients with gunshot wounds involving their tendon sheaths and a fourth case of ankylosis of the elbow. It is interesting that in this report he mentions the possible value of amniotic membrane in myolysis, neurolysis, and duraplasty. In a later communication⁶⁶ he described the successful recovery of function in a case of ankylosis of the knee joint treated by interposition of this material.

Lyman and Bergtold⁴⁰ used human amniotic membrane to prevent postoperative peritoneal adhesions in seven human cases. While they reported success, their conclusions were drawn entirely on clinical observation.

The successful use of amniotic membrane reported in these earlier papers apparently aroused but little enthusiasm. No further observations on this material are recorded until 1933, at which time Lyons⁴¹ reported the satisfactory epithelization of two postoperative mastoid cavities lined with fresh, sterile human amniotic membrane obtained at cesarean section. In 1937, Johnson³¹ reported good results with human amniotic membrane in avoiding adhesions between the traumatized peritoneal surfaces of rabbits. However, he noted³² that the membrane was treated as a foreign body by the contiguous tissues. In the same year Davis and Arics³⁴ reported their observations on beef and human amniotic membranes used for the prevention of adhesions around repaired nerves and tendons and between the denuded peritoneal surfaces of dogs. The nerve and tendon experiments were unsuccessful but excellent results were obtained in the peritoneal cavity.

Burger⁸ has described three cases of successful reconstruction of the human vagina with fresh fetal membranes obtained at cesarean section. He and his associates have also used living human fetal membranes to replace the dura in cats. He notes, "In one of the cases the adherence was satisfactory, still this lone case was not sufficient for the solution of our problem."

The first observations on the use of amniotic membrane to prevent adhesions between the brain and its coverings were those reported by Chao, Humphreys, and Penfield.¹² These workers reported success with amnioplastin, a specially prepared form of human amniotic membrane. The membrane was placed over the wounded cerebral cortex and leptomeninges of cats. The animals were killed at regular intervals up to sixty days. The membrane caused only a slight cellular reaction and was completely absorbed at the end of thirty days. Within this thirty-day period the pia-arachnoid had covered the cerebral wound, and adhesions to the overlying structures did not occur. Their consistently good results led these observers to recommend amnioplastin "as a preventative of meningocerebral adhesions and as an adjunct to radical surgery necessary to prevent post-traumatic and postoperative epilepsy."

In a later communication Penfield⁵² warned against use of amnioplastin until further studies had been carried out. This warning was issued principally because of his knowledge of the unsatisfactory results obtained by us with amnioplastin up to that time. The second factor was the unfavorable postoperative course in a case of focal epilepsy treated by covering the area of scar excision with amnioplastin. At the second craniotomy seven months later, dense connective tissue had bound the brain to the dura.

Recently several enthusiastic reports on the clinical use of amnioplastin have appeared in the literature. Garcin and Guillaume²⁴ have used it to repair dural defects associated with cranio-cerebral gunshot wounds. Rogers⁶² favors the use of this membrane following craniotomy and neurolysis. He records no observation on the tissue reaction to the membrane. Law and Philip³⁷ and de Röttth¹⁷ report that amnioplastin and human fetal membranes are of value in ophthalmologic surgery.

Methods and Materials.—In the earlier experiments human amniotic membrane was prepared in the manner outlined by Chao, Humphreys, and Penfield.¹² This requires the separation of the amnion from the chorion by finger dissection, washing in running water, fixation in 70 per cent alcohol, stretching and drying on a glass plate and finally, sterilizing in the autoclave for twenty minutes at 250° F. with 120 pounds' steam pressure.

Due to our disappointing results with the membranes so prepared, other techniques were used. For practical purposes we have classified the various membranes as fixed, fresh, and attenuated types.

Fixed Amniotic Membrane (Amnioplastin): Human amniotic membrane* obtained at delivery was subjected immediately to one of the following methods of preparation:

1. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; boiled, 20 minutes.

2. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

3. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; boiled, 20 minutes; 70 per cent alcohol, 9 days.

4. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; 70 per cent alcohol, 7 days; boiled, 20 minutes; 70 per cent alcohol, 24 hours.

5. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; 70 per cent alcohol, 15 minutes; boiled, 20 minutes; 70 per cent alcohol, 24 hours.

6. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 24 hours; 70 per cent alcohol, 4 days; boiled, 20 minutes; 70 per cent alcohol, 24 hours.

7. Washed in 70 per cent alcohol, 24 hours; boiled, 20 minutes.

8. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; 4 days in 60° C. oven; ether, 24 hours; boiled, 20 minutes; 70 per cent alcohol, 24 hours.

9. Washed in 70 per cent alcohol, 25 days.

10. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 5 days; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

11. Washed in 70 per cent alcohol, 24 hours; 95 per cent alcohol, 24 hours; absolute alcohol, 24 hours; ether, 5 days; boiled, 20 minutes.

*The fetal membranes were supplied through the generosity of the staff of the Royal Victoria Montreal Maternity Hospital.

12. Washed in 70 per cent alcohol, 1 hour; ether, 5 days; dried, 5 days; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

13. Washed in 70 per cent alcohol, 1 hour; ether, 5 days; dried, 5 days; boiled, 20 minutes.

14. Washed in ether, 6 days; dried; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

15. Washed in ether, 6 days; dried; boiled, 20 minutes.

16. Washed in ether, 4 days; 70 per cent alcohol, 10 minutes; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

17. Washed in ether, 4 days; 70 per cent alcohol, 10 minutes; boiled, 20 minutes.

18. Washed in 70 per cent alcohol, 10 minutes; ether, 5 days; 70 per cent alcohol, 20 minutes; autoclaved 20 minutes at 250° F., with 120 pounds' pressure.

19. Washed in 70 per cent alcohol, 10 minutes; ether, 5 days; 70 per cent alcohol, 20 minutes; boiled, 20 minutes.

20. Washed in 70 per cent alcohol, 20 minutes; ether, 9 days; 70 per cent alcohol, 5 minutes; dried, 4 days; autoclaved, 20 minutes at 250° F., with 120 pounds' pressure.

21. Washed in 70 per cent alcohol, 20 minutes; ether, 9 days; 70 per cent alcohol, 5 minutes; dried, 4 days; boiled, 20 minutes.

22. As outlined by LeVann.³⁹ Amnion separated from chorion, placed in acetone 15 hours, rinsed in 70 per cent alcohol, dried on rough toweling 24 hours, then immersed in ether 12 hours, rinsed in 70 per cent alcohol, dried 24 hours and sterilized in the autoclave.

Fresh Amniotic Membrane: The membranes were obtained at cesarean section, placed immediately in a sterile container, and kept in an incubator at 37° C. until ready for use. At the time of operation the amnion was separated from chorion by finger dissection, cut to the desired size, and placed on the brain. The time between cesarean section and implantation did not exceed three hours.

Attenuated Amniotic Membrane: Selected pieces of the fresh membrane were placed in sterilized tubes of liquid petrolatum and kept in a refrigerator at 3° C. for approximately one month before use. This is Huber's³⁰ method for storage of nerve grafts.

Experimental Results.—Without exception, the membranes were treated as foreign bodies by the tissues and enveloped in a connective tissue capsule of varying thickness. In the majority of experiments there was, in addition, a moderate degree of cellular reaction involving small round cells and a few foreign body giant cells. Occasionally this reaction was intense. Although the different methods of preparation did produce some variation in the thickness of the capsule, the cellular reaction, and the rate of resorption of the membrane, they did not appreciably alter the end results. Ultimately the cerebral wound became bound to the overlying dura by a connective tissue core (Fig. 3). Our earlier impression that the fat-free membrane would prevent adhesions proved to be false.

There are several stages in the encapsulation of the fixed membrane. Disintegration of the membrane begins in the epithelial layer and involves the collagen layer at a later period. Shortly after implantation

the epithelial cells become swollen and are eventually broken up into globular, amorphous material. The entire membrane was usually absorbed after thirty to sixty days. However, in several animals traces of it were still present at the end of four months. The membranes prepared in alcohol alone remained intact longer than the other types. Furthermore, the same piece of membrane was usually resorbed more slowly if it had been sterilized by boiling rather than in the autoclave. This would seem due to the shrinkage and thickening of the membrane caused by the boiling.

The connective tissue forming the capsule became adherent earlier to the collagen layer of the membranes. Adherence to the opposite surface was delayed until the epithelial cells had disappeared. Finally, with the onset of resorption of the collagen layer, connective tissue fibers traversed the clefts in the membrane and eventually fused the inner and outer layers of the capsule.

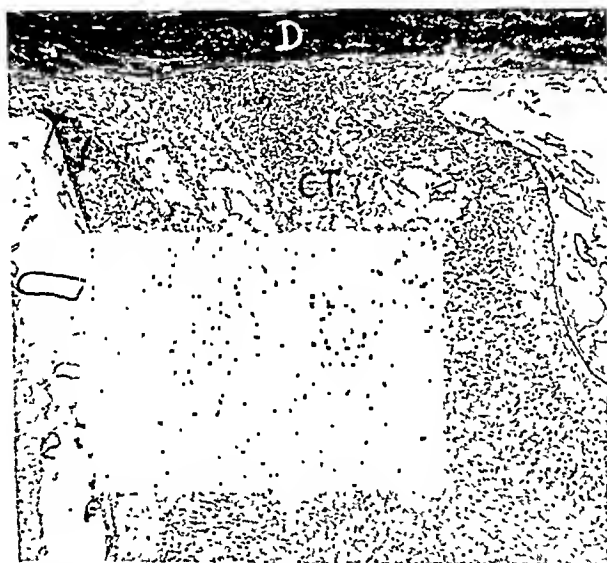


Fig. 3.—Result twenty-eight days after emplacement of amnioplastin; the membrane has disappeared. Dense connective tissue (CT) binds the cerebral wound (W) to the overlying dura (D). Hematoxylin and van Gieson stains.

There were but five encouraging results in the series of ninety-five cerebral wounds covered with amnioplastin. In four of these the animals had only delicate meningeocerebral adhesions on gross inspection. In these cases microscopic examination showed the cerebral wound to be partly bridged by the regrowth of pia-arachnoid. This carpet of leptomeningeal cells was interrupted centrally by the meningeocerebral band of connective tissue. The one good result occurred in a cat killed after 118 days. In this experiment there were no adhesions on gross inspection. However, microscopic examination dis-

closed a few filamentous strands which may have been broken during the process of removal or fixation.

Uniformly poor results were obtained with the fresh membranes. Both the capsule formation and the cellular reaction were extremely intense (Fig. 4). The dura and brain were tightly adherent through the medium of this capsule. Large aggregations of small round cells with clumps of foreign body giant cells were the principal components of the inflammatory reaction. The most interesting feature observed in these experiments with fresh membrane was the histologic evidence for viability of its collagen layer. Both the collagen fibers and the fibroblast nuclei dispersed among them, stained with a brilliance and distinctness comparable to that of the native connective tissue.

Use of the attenuated membranes likewise failed to prevent meningo-cerebral adhesions. However, the cellular reaction to this type of amniotic membrane was less than with the fresh and fixed forms. Encapsulation was slight and the reaction of inflammatory cells minimal (Fig. 5). Furthermore, the collagen layer of these membranes behaved like a viable material. It remained well preserved and eventually became incorporated as part of the connective tissue reaction investing it.



FIG. 4.—Fresh amniotic membrane after ninety-seven days. The capsule is adherent to the cerebral wound (W), a large aggregation of small round cells (SRC) is shown. Hematoxylin and van Gieson stains.

Allantoic Membrane

Historical Survey.—Beef allantoic membrane, known commercially as insulitoic membrane, was first employed for the prevention of adhesions by Johnson.³¹ He covered the denuded peritoneal surfaces of rabbits and traumatized tendons of calves with this material. The membrane stimulated a foreign body reaction and was eventually en-

capsulated. Nevertheless, his results were excellent due to the smoothness of the inner surface of the connective tissue capsules. Adhesions did not occur unless the membrane slipped or was of insufficient size to cover the traumatized area.

The excellent results obtained by Johnson have been confirmed by the work of Davis and Aries.¹⁴ These observers covered denuded peritoneal surfaces and the line of suture in nerves and tendons of dogs with allantoic membrane. Around the nerves and tendons this membrane was superior to the control materials, namely, beef and human amniotic membrane, sheet catgut, beef cecum, cellophane, and rubber latex. In the peritoneal cavity, however, better results were obtained with amniotic membrane, especially if its mucous surface was intact. The allantoic membrane prevented peritoneal adhesions only to the extent and size of the patch which was used.

Chao, Humphreys, and Penfield¹² had promising results with allantoic membrane for the prevention of meningeocerebral adhesions. The adhesions that formed were few in number and the cellular response slight. In view of their encouraging findings in a small number of experiments, a further study of this membrane seemed warranted.



Fig 5—Attenuated amniotic membrane (M) thirty days following implantation; encapsulation and cellular reaction are minimal. The inner layer of the capsule is adherent to the cerebral wound (W). Hematoxylin and van Gieson stains.

Methods and Materials.—This membrane is prepared from the allantois of the gravid bovine uterus.* Cattle and other ungulate (hoofed) mammals are an excellent source of this material. In these animals the allantois reaches a large size and serves as an embryonic organ of respiration, nutrition, and excretion. It is composed of a

*Allantoic membrane was supplied by the Lewis Mfg. Co., Brauer & Black, divisions of the Kendall Company, Chicago, Ill.

closed a few filamentous strands which may have been broken during the process of removal or fixation.

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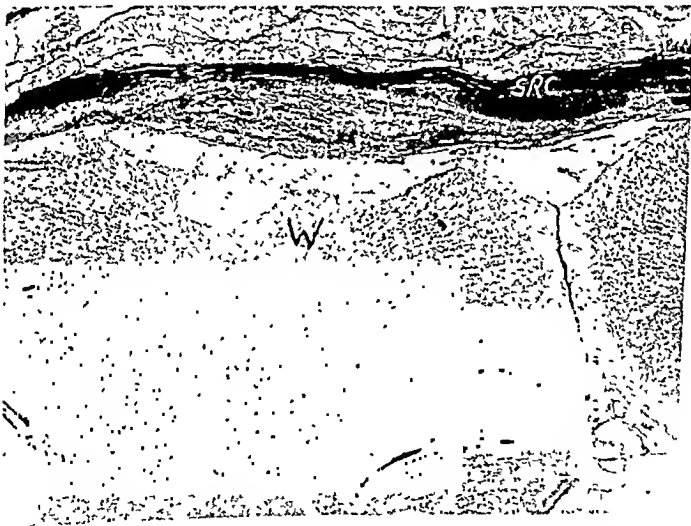


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thickness membranes were still recognizable in the sections at the end of eighty and eighty-five days, respectively, there was sufficient resorption at the end of sixty days to allow fibroblasts to proliferate through the clefts between the fragments. The experience with amnioplastin allows the assumption that when resorption of the membrane has been completed the cavity of the capsule would be entirely obliterated due to the fusion of its inner and outer walls. By this process the former plane of separation becomes the site of a firm attachment.

Cargile Membrane

Historical Survey.—In 1902, Morris⁴⁵ reported the use of prepared ox peritoneum for the prevention of postoperative peritoneal adhesions in human cases. He named this membrane in honor of Dr. Charles H. Cargile of Bentonville, Ark., who suggested its use. Morris reported good clinical results but subsequent observations on the condition of the membrane were not made.

Although Morris was a pioneer in the use of membranes of peritoneal derivation, he was preceded by Baum.² In 1894, Baum reported satisfactory clinical results following the use of the prepared peritoneum of freshly slaughtered calves to protect traumatized peritoneal surfaces. Later exposures of the membrane and protected surfaces were not mentioned.

In his original article Morris mentioned the close adherence of Cargile membrane to exposed brain tissue and intimated that it may be of value as temporary dura mater. He does not describe experiments to confirm this impression. Craig and Ellis¹³ were the first to attempt dural repair with Cargile membrane. They reported experiments in which this material was employed for dural restoration in dogs. Unfortunately, all of their results were vitiated due to suppuration in the wounds.

Prime⁵⁵ pioneered in the use of Cargile membrane for the specific purpose of preventing adhesions between the brain and its coverings. However, in his experiments the membrane was encapsulated and adhesions were invariable if the cortex was traumatized.

These early observations on Cargile membrane were followed by reports on other viable and nonviable membranes of peritoneal derivation. In practically all instances the purpose of the membrane was the closure of dural defects. Included in this group are membranes derived from hernia sacs, omentum, and the parietal and visceral peritoneal reflections. Satisfactory results have been obtained when these peritoneal membranes were used only as dural substitutes. Meningocerebral adhesions occurred invariably if the brain had been damaged.

Cargile membrane has been frequently recommended in the surgery of peripheral nerve injuries. In 1919, Joyce²² described the use of the prepared membrane of a fine variety to protect nerves following either suture or neurolysis. Four of his cases were re-explored three, four,

mesenchymal layer, containing a large number of blood vessels, and has an ectodermal lining.

For surgical use the membrane is prepared as follows. After a careful dissection of the membrane from the uterus it is cleaned by repeated washing in water. The membrane is then chromicized, stretched on gauze-covered boards, and dried. Pieces of the desired size are cut, placed in open tubes, and dehydrated in ovens. The method of sterilization is that employed for catgut, namely, immersion in light hydrocarbon oil for one hour at 155° C. Following this stage the oil is drained off and the tubes filled with 100 per cent ethanol containing 0.1 per cent of potassium mercuric iodide. Finally, the glass tubes are sealed and the membrane is ready for use.

Both the single and the double thickness chromicized membranes were used in the present series of experiments. They were thoroughly washed in physiologic saline solution prior to emplacement on the brain.

Experimental Results.—This membrane was used in five animals for periods of time varying from twenty-four to eighty-five days. In all of the experiments the membrane was treated as a foreign body and walled off by dense connective tissue (Fig 6). The inner layer of the capsule



Fig. 6—After sixty-three days single thickness allantoic membrane (*M*) is invested in dense connective tissue. The inner face of this capsule is bound to both the cerebral wound (*W*) and pia-arachnoid over the crown of the wounded gyrus. Hematoxylin and van Gieson stains.

was invariably adherent to the cerebral wound. A further evidence of tissue irritation was the presence of foreign body giant cells, small round cells, and phagocytes, at times in large numbers. The phagocytes were especially numerous during the period when resorption of the membrane was most active. Although both the single and double

of connective tissue between these fragments. Finally, the inner surface of the capsule was tenaciously adherent to the cerebral wound in all of the experiments

Tantalum

Historical Survey.—In 1940, Burke⁹ introduced tantalum, a new metal for surgical use. In contrast to the stainless steels and vitallium, both of which are alloys, tantalum is an element. Pure tantalum is bluish gray, soft, malleable and ductile. It is resistant to most organic reagents except those which contain fluorine, free sulfur trioxide, or strong alkalis.

Burke used tantalum in the form of bone plates and screws in dogs and rabbits, and as a skin suture in thirty-four human cases. In all of these instances there was a lack of tissue irritation. The observations of Burch and Carney⁷ on tantalum bone plates and screws and sutures are confirmatory. Recently, one of us (R. H. P.) has shown that strips of tantalum ribbon may be embedded in cerebral tissue without provoking an inflammatory reaction. In view of these findings it was believed that thin sheets of this metal would be of value in the prevention of meningocerebral adhesions.

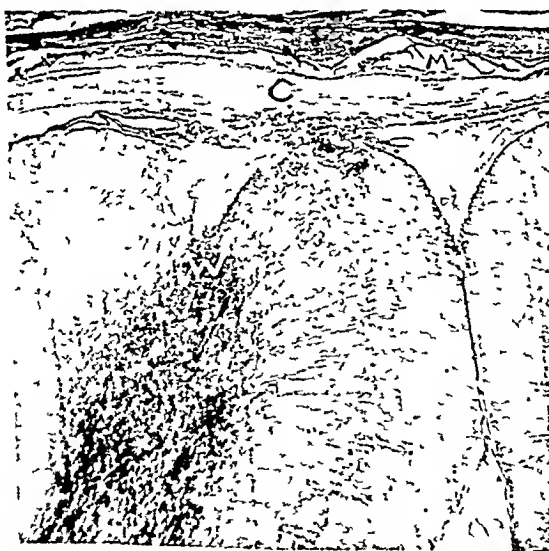


Fig 7.—Cargille membrane (M) after sixty days, the thick inner layer of the capsule (C) is intimately bound to the cerebral wound (W) by the connective tissue core. Hematoxylin and van Gieson stains

Methods and Materials.—Tantalum foil* of 0.001 of an inch thickness was used. A thinner foil is preferable but impossible to obtain. Due to the physical characteristics of the grain structure of this metal, fully annealed, homogeneous sheets less than 0.001 of an inch in thickness cannot be rolled

*Courtesy of the Lanston Metallurgical Corporation, North Chicago, Ill.

seven, and nineteen months later. From his observations on these cases he concluded that the membrane is absorbed in less than six months. During this time it fulfils its purpose as a protective against adhesion formation.

Huber³⁰ also reported satisfactory results following the use of Cargile membrane. The commercial type of membrane was absorbed in ten days and felt to be unsatisfactory. However, if this material was placed in 70 per cent, followed by absolute, alcohol and then dried, his results were better. The alcoholized membrane was not absorbed within five to six months and during this time protected the nerve and incited only a minimal connective tissue reaction. His results with formalized arterial sheaths, fat, and fascia lata were much less satisfactory. Cairns and Young¹⁰ considered the fresh membrane as being superior to the alcoholized form. They remark that the latter type causes a greater tissue reaction around the nerve.

In addition to his experimental studies of amniotic and allantoic membranes, Johnson³¹ employed Cargile membrane to prevent peritoneal adhesions. In all of his experiments the membrane was treated as a foreign body and the results were uniformly poor.

Chao and his co-workers¹² used Cargile membrane in their studies of the prevention of meningocerebral adhesions in cats. They found dense adhesions and a moderate cellular response in all of the experiments.

In summary, therefore, the experience with Cargile membrane over the wounded brain and peritoneum has been generally unsatisfactory. Nevertheless, due to the availability of large amounts of this material, the promise it has shown in peripheral nerve surgery and the lack of adequate study of its usefulness in the prevention of meningocerebral adhesions, we have subjected it to further investigation.

Methods and Materials.—The commercial, unchromicized Cargile membrane* was employed. This membrane is derived from the submucous layer of the ox cecum. It is prepared according to the method used for catgut, namely, washing, drying, and sterilization by heating in a light hydrocarbon oil. The result of this process is a thin, translucent, and pliable membrane that conforms nicely to the convolutional pattern of the brain over which it is placed.

Experimental Results.—Cargile membrane was used in five cats. The animals were killed at intervals extending from four to ninety days. These membranes have failed to prevent meningocerebral adhesions in all of the experiments. The type of reaction is essentially similar to that noted with insultic membrane. Again there is formation of a dense connective tissue capsule (Fig. 7) and a variable inflammatory cell pattern involving foreign body giant cells, small round cells, and phagocytes. At the end of sixty days the membrane had undergone only slight resorption. However, at the end of ninety days it was fragmented and the cavity of the capsule bridged by the proliferation

*Kindness of Johnson & Johnson, New Brunswick, N. J.

vinyl alcohol compounds. These substances are used commercially in the manufacture of shatterproof glass. Their chief attraction in the present study is the change in the solubility rate obtainable by modifying their structural formulas. The replacement of the hydroxyl groups of polyvinyl alcohol with acetate groups eventually changes the compound to polyvinyl acetate. The compounds formed in the stages of transition vary in their solubility. Maximum solubility is obtained when approximately 20 per cent of the hydroxyl groups have been replaced by acetate groups. Pure polyvinyl alcohol and polyvinyl acetate are less soluble than this 20 per cent compound. One, therefore, has the choice of these substances in a wide range of solubility.

In 1938, Dötzer¹⁸ reported experiments on the reactions of bacteria in contact with polyvinyl alcohol. Colon bacilli, streptococci, staphylococci, pneumococci and tubercle bacilli were inoculated in nutrient media containing either pure polyvinyl alcohol or polyvinyl alcohol, with hydroxyquinoline potassium sulfate added in concentrations of 0.1 per cent and 0.16 per cent. Pure polyvinyl alcohol was found to be bacteriostatic but not bactericidal. However, with the addition of the small amounts of antiseptic, most of the bacteria were killed when the ratio of polyvinyl alcohol to culture media was 1:1 and all were killed when this ratio was 10:1. In his report Dötzer mentions the animal experiments of Braun and Herrmann in which polyvinyl alcohols were used. Unfortunately the results of these experiments are not described.

Methods and Materials.—In the problem under consideration the most favored compound would be the one which would remain intact for at least one month. This length of time would permit the pia-arachnoid to carpet a small cerebral wound without the interference of invading connective tissue cells derived from the dura and other overlying structures. On the basis of solubility in human cerebrospinal fluid in vitro at 37° C., a polymerized vinyl alcohol* having a 5 per cent replacement of hydroxyl groups with acetate groups and a viscosity of 15 centipoises was selected.

The material was made into extremely thin, transparent films resembling a fine grade of cellophane. These films were inserted between sheets of filter paper, placed over a water bath, and sterilized in an electric oven at 100° C. for forty-five minutes. The absence of bacteria in the films was confirmed by aerobic and anaerobic culture. Prior to their use on the cerebral cortex, the sheets were moistened in physiologic saline solution.

Experimental Results.—The 5 per cent polyvinyl alcohol films were used in five animals. The period of observation varied from ten to sixty-six days. In all of the experiments the results were disappointing. Invariably, the membrane was invested in a thick connective capsule, the inner surface of which was firmly adherent to the cerebral

*Courtesy of Shawinigan Chemicals Ltd., Shawinigan Falls, P. Q.

The pieces of foil, cut to the desired size, were sterilized either by boiling or autoclaving. Before the sheets were applied to the brain surface they were bent to conform to the cortical contour and all sharp corners were rounded off.

Experimental Results.—The reactions to tantalum foil have been observed in six animals over a period ranging from 10 to 143 days. In all of the experiments there has been only a minimal reaction of connective tissue and other cellular elements. Encapsulation has been comparatively slight. The attachment between the cerebral wound and overlying dura has been an indirect one by way of the margin of this capsule (Fig. 8). Giant cells were found in one of the experiments but were few in number. There was no reaction involving small round

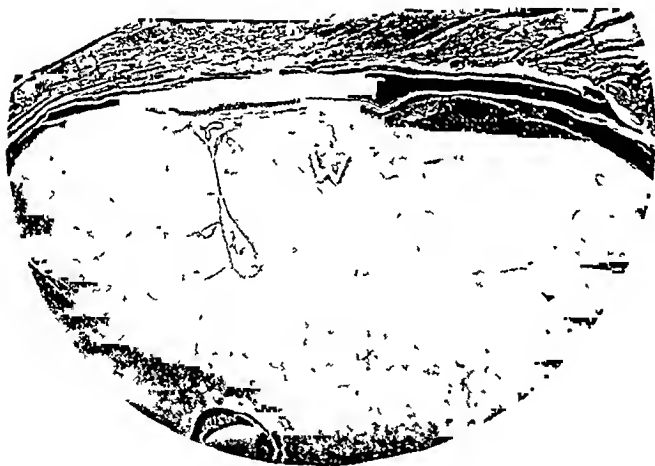


FIG. 8—Result thirty days following implantation of tantalum foil, the inner layer of the capsule previously occupied by the tantalum (T) is adherent to the cerebral wound (W). Hematoxylin and van Gieson stains.

cells, polymorphonuclear leucocytes, or phagocytic cells. In one animal killed at the end of seventy-nine days, the capsule formation was exceptionally slight and the cerebral wound was bridged by a membrane histologically identical with the arachnoid. The removed pieces of tantalum had their original luster. There was no evidence that any corrosion had occurred.

Polyvinyl Alcohol

Historical Survey.—The search for materials in which the rate of resorption in the tissues could be controlled disclosed the polymerized

ready bridged the cerebral wound. Other than a few foreign body giant cells noted in the capsular space in one experiment, there was no inflammatory reaction. Furthermore, the removed pieces of foil had their original luster, suggesting a complete absence of corrosion in the tissues.

The resorbable membranes, namely amnioplastin, allantoic membrane, and Cargile membrane, may be considered as a group since the response of the tissues to all of them is essentially similar. The thickness of the capsule investing these membranes is modified by two factors, namely, the extent of wrinkling, and the resorption time of the membrane. The folds of the wrinkled membrane are invaded by fibroblasts with a resulting greater thickness of the capsule in these areas. In general, the capsule formation was a continued proliferation of connective tissue which did not cease until the membrane disappeared. Amnioplastin was absorbed more quickly than the other materials, usually requiring thirty to forty days. If left in alcohol for several days before use, or boiled instead of autoclaved, it required a longer period of time. The epithelial layer disappeared more quickly than the connective tissue stratum. Chromicized single and double thickness allantoic membranes were histologically demonstrable in the tissues at the end of eighty and eighty-six days, respectively, but were fragmented and undergoing active resorption. Cargile membrane was for the most part intact at the end of ninety days, although phagocytosis had commenced and fragmentation was rather extensive.

As noted previously, the onset of fragmentation and resorption of these membranes was followed by proliferation of the cells lining the capsular space with eventual fusion of the inner and outer walls. The absorbable membranes have, therefore, not only failed to prevent meningeocerebral adhesions but have provoked a reaction probably greater than would have occurred had they not been used. Lastly, all of these materials have stimulated an inflammatory reaction with a variable pattern involving foreign body giant cells, small round cells, and phagocytes. In the experiments with amnioplastin the inflammatory reaction was greater on the epithelial side of the membrane.

It is obvious from the large number of experiments on amnioplastin that the chief purpose of this study was to determine whether or not the continued clinical use of this material was justified. We now believe that the use of this material for the prevention of meningeocerebral adhesions is not warranted. It is difficult to account for the discrepancies between the results obtained by Chao, Humphreys, and Penfield¹² and the findings in the present study. In our earlier experiments the technique for preparation of the amnion, as outlined by these authors, was rigidly followed. The finding of meningeocerebral adhesions in all of the experiments with the membrane so prepared led to the many other methods of fixation, fat extraction, sterilization, and preservation. Furthermore, the emplacement of the membrane over the

wound. Giant cells were particularly prominent in the inflammatory reaction (Fig. 9). Aggregations of phagocytes and small round cells were scattered throughout the capsule. In addition, pools of homogeneous material, which stained a bright pink with acid fuchsin, were found in the capsular interstices. At the end of 66 days the membrane was for the most part intact but showed a moderate amount of swelling suggesting beginning resorption.

DISCUSSION

While this study has failed to disclose an ideal material for the prevention of meningocerebral adhesions, it is not without value. In addition to confirming or denying the results of past workers, it has disclosed certain factors which must be considered in the ultimate solution of the problem.

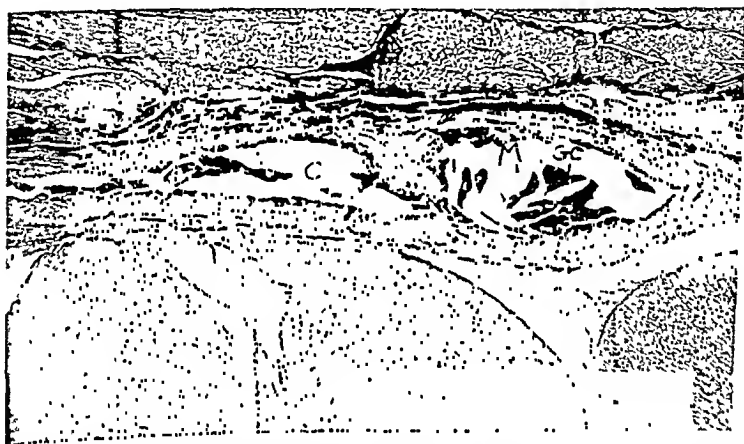


Fig. 9.—Dense encapsulation (C) and cellular reaction surrounding the polyvinyl alcohol membrane (M); the capsule is adherent to the cerebral wound (W). Giant cells (GC) are prominent. Period of observation, sixty-six days; hematoxylin and van Gieson stains.

All of the materials, without exception, have been encapsulated. This capsule is derived principally from the dura and to a lesser extent from the arachnoid. Its pattern, thickness, and cellularity have varied with the material used. As long as the membrane remains intact the inner and outer layers of the capsule are separable. However, with the onset of resorption, fibroblasts grow through the defects in the membrane, fuse the inner and outer connective tissue walls, and eventually obliterate the capsular space. In addition to the fibroblastic activity, there has been an inflammatory reaction which has varied with each material. The character of the individual reactions may now be considered.

Tantalum foil was superior to all of the materials employed. Encapsulation of the metal was comparatively slight even at the end of 143 days. In an animal killed after seventy-nine days the inner layer of the capsule consisted of slightly thickened arachnoid which had al-

sanction or condemn their use in other surgical procedures. Satisfactory results with many of these substances have been reported by other observers. Furthermore, a detailed study of any one material, other than amnioplastin, has not been carried out. Nevertheless, we wish to re-emphasize that in our studies all of these materials, both resorbable and nonresorbable, were treated as foreign bodies and encapsulated in connective tissue. Furthermore, resorption of the membranes was followed by a fusion of the inner and outer layers of this capsule. Due to these factors, the membranes not only failed to prevent meningo-cerebral adhesions but probably contributed to their formation.

SUMMARY AND CONCLUSIONS

The experiments in this study concern the development of a material for use in the prevention of adhesions between the wounded brain and its coverings. The investigation was stimulated by the high incidence of epilepsy following open craniocerebral injuries, particularly those due to missiles. In the introduction we have discussed the theoretical significance of the meningeal ingrowth of cerebral scar in the causation of post-traumatic epilepsy. The literature bearing on the problem is reviewed.

Seven different materials, namely, human amniotic membrane in fresh, attenuated and fixed (amnioplastin) forms, beef allantoic (Insultic) membrane, Cargile membrane, sheets of the metal tantalum .001 inch in thickness, and films of 5 per cent polyvinyl alcohol were used. These substances were placed over both the wounded and unwounded cerebral hemispheres of a large number of cats. The animals were killed at appropriate intervals varying from 4 to 240 days. Gross and microscopic observations of the tissue reactions to the materials are reported. The following conclusions are drawn:

1. All of these materials are foreign bodies and are eventually encapsulated. The connective tissue and inflammatory cell reaction are variable in intensity. Although a few of them show promise, none can be considered as having offered a solution to the problem.

2. Tantalum foil was surprisingly inert and provoked but minimal encapsulation and inflammatory reaction. Being an impermeable material the meningo-cerebral attachment was an indirect one via the margin of the capsule.

3. With the resorbable membranes, namely, amnioplastin, insultic membrane, and Cargile membrane, the connective tissue investment and inflammatory cell response were more pronounced. Resorption of these materials was followed by fusion of the inner and outer layers of the capsule with resultant binding of the brain and dura through the medium of dense connective tissue.

4. The fresh and attenuated amniotic membranes did not prevent meningo-cerebral adhesions but are of interest because of the histologic evidence for survival of their connective tissue layers.

cerebral wound was controlled so that we knew if the epithelial or connective tissue layer was in contact with the brain.

There was but one good result in the ninety-four experiments with amnioplastin. This animal was killed at the end of 118 days. The membrane had been prepared by fixation in a series of alcohols, extraction of the fat in ether, drying, and autoclaving. Membranes prepared in exactly the same way produced adhesions in other animals.

When last heard from in April, 1940, Chao, in Peiping, was still enthusiastic about amnioplastin. He had used the material in a series of operations on human cases and believed that it was satisfactory. Unfortunately, due to the war, no further correspondence has been received and we are unaware of his present impression of this material.

Both the fresh and attenuated forms of amniotic membrane have failed to prevent meningocerebral adhesions. Nevertheless, certain observations on these materials are worthy of mention. The most interesting feature is the histologic evidence for the viability of their connective tissue layers. The collagen fibers were sharply demarcated with the characteristic large, oval, vesicular nuclei of fibroblasts scattered among them. There was no evidence that these nuclei belonged to fibroblasts which had infiltrated from the adjacent tissues.

The chief difference between the fresh and attenuated amnion lies in the reaction of the surrounding tissues to their presence. Large aggregations of polymorphonuclear leucocytes or small round cells were constantly present along both surfaces of the fresh membrane, particularly on the epithelial side. The response of the encapsulating connective tissue cells was similarly intense. In contrast, the attenuated membrane provoked but minimal capsule formation and inflammatory reaction. Other than a few aggregations of small round cells in one experiment, inflammatory cells were lacking. The method of attenuation had apparently inactivated the irritating factor in the fresh membrane.

In all of the experiments the implantation of the polyvinyl alcohol films was followed by encapsulation in dense connective tissue and an intense inflammatory reaction involving cells of many types. The reaction has been more severe than with any of the other materials. The films were still intact at the end of sixty-six days, a much longer time than was anticipated. It is possible that a more soluble compound would have been less irritating.

From the practical standpoint, therefore, none of the materials can be recommended for permanent use over the wounded brain. Tantalum foil and the resorbable animal membranes may be practical for the temporary separation of layers, for example, between stages of a two-stage craniotomy. If used for this purpose it would be necessary to carry out the second stage before appreciable resorption had occurred.

Since our study has been limited to the use of these materials for the prevention of meningocerebral adhesions alone, we are not qualified to

25. Glaser, M. A., and Thienes, C. H.: Dural Defects. How Important Is Their Surgical Repair? Experimental Study Upon Heteroplastic and Autoplastic Dural Grafts, *California & West. Med.* 48: 163-166, 1938.
26. Greer, W. J.: Craniotomy With the Implantation of Egg-Shell Membrane for Jacksonian Epilepsy, *Bristol Med.-Chir. J.* 19: 42-44, 1901.
27. Hanel: Ueber alloplastischen Duraersatz, *Arch. f. klin. Chir.* 90: 823-828, 1909.
28. Hantsch, V.: Plastic Operations on Dura and Skull, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 34: 328-333, 1921.
29. Harris, M. L.: The Use of Silver Foil to Prevent Adhesions in Brain Surgery, *J. A. M. A.* 42: 763-765, 1904.
30. Huber, G. C.: Repair of Peripheral Nerve Injuries, *Surg. Gynec. & Obst.* 30: 464-471, 1918.
31. Johnson, H. L.: Insulating Patches and Absorbable Sutures Made from Fetal Membranes, *New England J. Med.* 216: 978-982, 1937.
32. Johnson, H. L.: Personal Communication.
33. Joyce, J. L.: A Study of a Series of Peripheral Nerve Injuries From a Surgical Aspect, *Brit. J. Surg.* 6: 418-457, 1919.
34. Kirschner, M.: Zur Frage des plastischen Ersatzes der Dura Mater, *Arch. f. klin. Chir.* 91: 541-542, 1909.
35. Kirschner, M.: Quoted by Krause, F., and Schum, H.: In "Die Spezielle Chirurgie der Gehirnkrankheiten," Stuttgart, 1932, Ferdinand Enke, vol. 2, p. 731.
36. Körte, W.: Quoted by Krause, F., and Schum, H.: In "Die spezielle Chirurgie der Gehirnkrankheiten," Stuttgart, 1932, Ferdinand Enke, vol. 2, p. 731.
37. Law, B. B., and Philip, J. F.: Amnioplastin as a Conjunctival Graft, *Brit. M. J.* 1: 514, 1941.
38. Lear, M., and Harvey, S. C.: The Regeneration of the Meninges—The Pia-Arachnoid, *Ann. Surg.* 80: 536-544, 1924.
39. LeVann, L. J.: Amniotic Membrane for Cerebral Adhesions, *Brit. M. J.* 1: 213, 1941.
40. Lyman, C. B., and Bergtold, W. H.: Amniotic Membrane for the Prevention of Postoperative Peritoneal Adhesions—A Preliminary Note, *Surg., Gynec. & Obst.* 18: 762-763, 1914.
41. Lyons, H. R.: Use of Amniotic Membrane as a Transplant in Radical Mastoidectomy, *Tr. Am. Laryng., Rhin. & Otol. Soc.* 39: 11-13, 1933.
42. McCosh, A. J.: Trephining and Heteroplasty for Traumatic Epilepsy, *Ann. Surg.* 27: 670-671, 1898.
43. McCosh, A. J.: The Surgical Treatment of Epilepsy—With a Report of Fourteen Cases, *Am. J. M. Sc.* 115: 549-573, 1898.
44. Morehead: Quoted by Coe in the discussion of the paper by Estes, W. L., 1896.
45. Morris R. T.: A Report on Experiments Made With the Cargile Membrane for the Purpose of Determining Its Value in Preventing the Formation of Peritoneal Adhesions, *M. Rec.* 61: 773-775, 1902.
46. Oberniedermayr, A.: Alloplastischer Duraersatz, *Arch. f. klin. Chir.* 150: 667-675, 1928.
47. Oelsner, A., and Garside, E.: Peritoneal Adhesions—Their Prevention by the Use of Digestive Ferments, *Surg., Gynec. & Obst.* 54: 338-361, 1932.
48. Oliver, J. C.: Cerebral Surgery: Report of Cases, *J. A. M. A.* 26: 1061-1065, 1896.
49. Penfield, W.: Meningocerebral Adhesions, *Surg., Gynec. & Obst.* 39: 803-810, 1924.
50. Penfield, W.: The Mechanism of Cicatricial Contraction in the Brain, *Brain* 50: 499-518, 1927.
51. Penfield, W.: Epilepsy and Surgical Therapy, *Arch. Neurol. & Psychiat.* 36: 449-484, 1936.
52. Penfield, W.: Amnioplastin—A Warning, *Brit. M. J.* 2: 668, 1940.
53. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, ed. 1, Springfield, 1941, Charles C Thomas.
54. Penfield, W.: Personal Communication.
55. Prime, F.: The Prevention of Post Operative Adhesions Between the Cortex and Dura, *Univ. Penn. M. Bull.*, 22: 57-61, 1909.
56. Rawling, L. B.: The Remote Effects of Gunshot Wounds of the Head, *Brit. J. Surg.* 10: 93-126, 1922.
57. Ray, J. H.: Epilepsy Treated by Subdural Implantation of Silver Foil, *Brit. M. J.* 1: 518, 1901.
58. Rehn, E.: Die Verwendung der autoplastischen Fett-transplantationen bei Dura und Hirndefekten, *Arch. f. Lhn. Chir.* 101: 962-996, 1913.

5. The 5 per cent polyvinyl alcohol films caused an intense inflammatory and fibroblastic reaction. However, this may be due to the fact that the compound used in this study was too insoluble.

6. Tantalum foil and the resorbable membranes (amnioplastin, alantoic, and Cargile membrane) may be of value for the temporary separation of layers, e.g., in a two-stage craniotomy. Use of these materials for permanent emplacement over the wounded brain is not recommended.

The authors wish to express their gratitude to Dr. Wilder Penfield, whose encouragement and guidance throughout this study have been invaluable.

REFERENCES

1. Abbe, R.: Epilepsy From Cortical Cicatrix; Trephining; Subdural Implantation of Rubber Tissue, *Ann. Surg.* 25: 95-96, 1897.
2. Baum, F.: How to Avoid Adhesions in Abdominal Sections, *J. A. M. A.* 23: 242, 1894.
3. Beach, H. H. A.: Compound, Comminuted Fracture of the Skull; Epilepsy for Five Years, Operation, Recovery. *Boston M. & S. J.* 122: 313-315, 1890.
4. Beach, H. H. A.: Gold Foil in Cerebral Surgery, *Boston M. & S. J.* 136: 281-282, 1897.
5. Brining, A.: Beitrage zur Duraplastik, *Deutsche Ztschr. f. Chir.* 113: 412-417, 1911.
6. Buné, J. M.: Ueber Duraplastik, *Beitr. z. klin. Chir.* 157: 9-34, 1938.
7. Bureh, J. C., and Carney, H. M.: Personal communication.
8. Burger, C.: The Biologic Significance of the Fetal Membranes, *Am. J. Obst. & Gynec.* 37: 572-584, 1939.
9. Burke, G. L.: The Corrosion of Metals in Tissues and an Introduction to Tantalum, *Canad. M. A. J.* 43: 125-128, 1940.
10. Cairns, H., and Young, J. Z.: Treatment of Gunshot Wounds of Peripheral Nerves, *Lancet* 2: 123-125, 1940.
11. Caporale, L., and de Bernardis, M.: Sur les hétéroplasties Durales avec le Catgut Lamincé, *Rev. de chir., Paris* 74: 10-27, 1936.
12. Chao, Y. C., Humphreys, S., and Penfield, W.: A New Method of Preventing Adhesions. The Use of Amnioplastin After Craniotomy, *Brit. M. J.* 1: 517-519, 1940.
13. Craig, A. B., and Ellis, A. G.: An Experimental and Histological Study of Cargile Membrane, *Ann. Surg.* 41: 801-822, 1905.
14. Davis, L., and Aries, L. J.: An Experimental Study Upon the Prevention of Adhesions About Repaired Nerves and Tendons, *SURGERY* 2: 877-888, 1937.
15. de Bernardis, M.: Plastiche Durali ed Evoluzione Sperimentale dello Ferite Craniomeningo-cerebrali, *Arch. ital. di chir.* 41: 255-359, 1935.
16. Denk, W.: Ueber die Beziehungen von organischen Veränderungen der Hirnrinde zur symptomatischen Epilepsie. Zugleich ein Beitrag zur Duroplastik, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 27: 827-858, 1914.
17. de Rötth, A.: Plastic Repair of Conjunctival Defects With Fetal Membranes, *Arch. Ophth.* 23: 522-525, 1941.
18. Dötzer, W.: Polyvinylalkohol als Material für Lungenplomben, *Zentralbl. f. Chir.* 65: 2661-2664, 1938.
19. Estes, W. L.: The Use of Gold Foil in Fractures of the Cranium and Resulting Hernia Cerebri, *J. A. M. A.* 26: 661-663, 1896.
20. Finsterer, H.: Ueber den plastischen Duraersatz und dessen Bedeutung für die operative Behandlung der Jackson-Epilepsie, *Beitr. z. klin. Chir.* 66: 193-206, 1910.
21. Finsterer, H.: Die Bedeutung der Duraplastik bei der Behandlung der Epilepsie nach geheilten Schädelschüssen, *Deutsche Ztschr. f. Chir.* 146: 145-207, 1918.
22. Foerster, O., and Penfield, W.: The Structural Basis of Traumatic Epilepsy and the Results of Radical Operation, *Brain* 53: 99-119, 1930.
23. Freeman, L.: Use of Egg Membrane in Trephining Operations Upon the Skull, *Ann. Surg.* 28: 455-457, 1898.
24. Garcin, R., and Guillaume, J.: Note sur le Traitement des blessures cranio-cérébrales par projectiles de guerre et sur les résultats obtenus par l'application des méthodes neurochirurgicales modernes dans une formation de l'avant. *Mém. Acad. de chir.* 66: 124-136, 1940.

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TRENDS IN THE TREATMENT OF BURNS

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IT IS timely to discuss trends in the treatment of burns, especially in view of the need of such treatment created by the war. This is, in many respects, a different kind of war than World War I and, while casualties from many causes are to be expected, the number suffering from severe burns is bound to be much higher. Naval engagements closely associated with oil and gasoline as well as stores of explosives and other inflammable materials may be frequent. The mechanization of troops adds other burn hazards, even if flame throwers are not used. Tank warfare and air fighting also impose thermal hazards not usual in open infantry or trench warfare.

Civilian populations may be subjected not only to the danger of falling buildings and explosions, but also to fires. It is quite likely that, unlike other wars where pestilence or trauma from projectiles took the toll of lives, in this war thermal injuries will account for the greatest loss of life and limb.

The history of burn therapy is interesting. The Chinese, about the sixth century B.C., treated burns by the use of strong infusions of tea. Hippocrates left four burn prescriptions to be used as liniments, with all but one containing some form of fat. Carron oil, which has been used by many in our generation, is similar to the mixture of lime water and oil advocated by Cerepion in the third century B.C. The many other forms of therapy advocated are too numerous to mention although reference should be made to ambrin, a mixture of paraffin and amber oil, no doubt an improvement on the melted paraffin advocated by Lawson Tait, in 1864. Ambrin was used during World War I and for some time thereafter. In fact, William Sherman of Pittsburgh is still a strong advocate of this type of local application.

59. Richardson, E. H.: Studies on Peritoneal Adhesions, *Ann. Surg.* 54: 758-797, 1911.
60. Rio-Hortega, P. del, and Penfield, W.: Cerebral Cicatrix—The Reaction of Neuroglia and Microglia to Brain Wounds, *Bull. Johns Hopkins Hosp.* 41: 278-303, 1927.
61. Ritter, C.: Beiträge zur Gewebstransplantation, *Med. Klin.* 663-665, 1910.
62. Rogers, L.: Experiences in Treatment of Peripheral Nerve Injuries with Amnioplastin, *Brit. M. J.* 1: 587-589, 1941.
63. Rohde: Cited by Buné, reference 6.
64. Sayad, W. Y., and Harvey, S. C.: The Regeneration of the Meninges—The Dura Mater, *Ann. Surg.* 77: 129-141, 1923.
65. Schmerz, H.: Ueber die Verwendung von Amnion als plastisches Interpositions-material, *Beitr. z. klin. Chir.* 73: 342-351, 1911.
66. Schmerz, H.: Ueber operative Kniegelenksmobilisierung und Funktionsherstellung durch Amnioninterposition, *Beitr. z. klin. Chir.* 76: 261-282, 1911.
67. Sehou, H. I.: Trauma Capitis and Epilepsy, *Acta. psychiat. et neurol.* 8: 75-78, 1933.
68. Summers, J. E.: Epilepsy Probably Cured and Paralysis Improved by Relieving Irritation and Compression Resulting From an Old Compound Depressed Fracture of the Skull, Replacing the Large Area of Depressed Fragments by Heavy Gold Foil, *Med. Rec.* 51: 590-591, 1897.
69. von Saar, G. F.: Ueber Duraplastik. Eine klinisch-experimentelle Studie, *Beitr. z. klin. Chir.* 69: 740-794, 1910.
70. Wagstaffe, W. W.: The Incidence of Traumatic Epilepsy After Gunshot Wounds of the Head, *Lancet* 2: 861-862, 1928.
71. Woolsey, G.: Gold Foil in Trephine Opening in the Skull, *Ann. Surg.* 25: 630-632, 1897.

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Blood chemical studies carried out in our patients at the Children's Hospital led to the recognition that in severe burns the blood chlorides were lowered. As emphasized by Davidson this finding resulted in attempts to increase fluid intake, and while in many instances edema resulted from too vigorous introduction of saline solution, some advantage was gained. A better understanding of the principles underlying the control of dehydration as outlined by Collier and Maddock have permitted us to control this difficulty. Transfusions of whole blood have been given to most of our patients to control reduction in blood volume. While Cumin, in 1823, noted hemoconcentration in relation to severe burns, the work of Underhill and his associates demonstrated this fact conclusively. Recognition of this important fact in relation to burns has resulted in additional lowering of mortality since plasma has become available for combating hemoconcentration.

While the introduction of tannic acid undoubtedly played an important role in advancing our understanding and treatment of changes in volume and composition of the blood resulting from burns, it also reduced the incidence and severity of secondary infection. Infections did occur, however, and when confined beneath the tannic acid crust were likely to be more troublesome than otherwise. Failure to adhere to basic surgical procedures in the preparation of the burned area has led to adverse criticism of the tannic acid method used in the treatment of the diffuse burns seen in civil life. While careful cleansing of the surface and débridement before the application of tannic acid reduces the tendency to infection, it must not be expected to be perfect.

Accordingly, the introduction of the sulfonamide compounds has been of great assistance in controlling, as well as combating, infection. During the period 1939 to 1942, 266 patients classified as hospital cases with moderately severe or severe burns were treated and of this number, it was deemed wise to administer one of the sulfonamide drugs to ninety-two patients. Fewer than ten patients had the drug applied locally, the majority being treated orally or intravenously. Absorption from the burned area may be great, and we have been careful with the use of sulfonamides locally in extensive burns in small children. We have used sulfadiazine, sulfanilamide, and sulfathiazole locally, and feel the use in this manner has merit. For the control and maintenance of adequate blood levels we have depended upon oral administration of the drug.

At the Children's Hospital of Michigan, my associates and I have been actively interested in this subject since the last war. The treatment of a burn, shortly after the last war, represented one of the most harrowing experiences, not only for the patient but for the surgeon as well. Raw, open, irritated, and painfully infected surfaces were the rule. Vaseline gauze, through which granulations grew, was painfully removed and painfully applied. Ambrin, used during the war period, gained recognition in civilian practice and to some extent alleviated the pain and suffering. The morale of the patient treated by either a moist dressing or vaseline gauze was difficult to maintain and no wonder, since the morale of the doctor was usually at its lowest ebb before he drove himself to the task. Such a state of affairs, while not always the same in detail, was similar in principle in all hospitals. The practice of the individual clinician or hospital was founded on routines dictated by experience and the results were assumed to be satisfactory. However, information gained from statistical studies showed the results to be far from gratifying. The morbidity was prolonged and the mortality was as high as 30 to 40 per cent.

It may be assumed at the outset that the ideal form of therapy is probably not at hand and there is much to be desired. The field for development is broad. The greatest modern advance in the treatment of burns was the introduction of the tannic acid treatment by Davidson, in 1925. Wells has stated that, "the introduction of tannic acid by Davidson has revolutionized and, apparently for the first time in history, standardized the treatment of diffuse burns." This contribution has not only relieved suffering and saved lives, but has influenced and stimulated others in their research on thermal injuries. The year 1925 marks an era, and we might with propriety think of the treatment of burns from a historic standpoint as the pre- or post-Davidson period.

The pre-Davidson period was not necessarily a period of bad treatment but rather one of varying and unstandardized methods. The burns seen regularly by any one physician were not many, and the development of basic understanding as well as standardized methods was not readily established.

As an evidence of the variations in treatment of the burned area I wish to recount some of my own experiences in the pre-Davidson period. In this period the mortality was high and the beginning of the post-Davidson period was ushered in by a marked drop in the mortality. In our series, shortly after World War I at the Children's Hospital the treatment consisted of a great variety of local applications such as boric acid and saline moist dressings, ambrin, vaseline gauze, exsanguination and transfusion after the idea advanced by Robertson, picric acid, scrubbing the burned area thoroughly with the patient anesthetized, saline solution and soda bicarbonate baths, and even the application of a solution of novocain.

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It is not our purpose to present statistics concerned with any one phase of the burn problem. We cannot refrain, however, from indicating again the general trend in our mortality statistics with advances in treatment. While there is no doubt that our greatest decrease in mortality came with the introduction of tannic acid, we wish to emphasize that it is not our belief that tannic acid in itself is the only important factor in the lowered mortality. Attention to surgical principles and general constitutional changes is also of prime importance. We have not adhered strictly to the use of tannic acid at the Children's Hospital but during the past several years we have used many other local applications, such as silver nitrate with tannic acid, triple dye, and gentian violet; saline baths and soaks; vaseline or scarlet red gauze; sulfadiazine in triethanolamine and sulfathiazole in an animal-fat base.

The recognition of basic problems associated with burns has contributed to the steady march of progress as exemplified by the care of the burned patient. The need for control of changes in the constituents of the blood as well as the recognition of the need for care in handling the burned surface and the control of infection seem obvious today. In the pre-Davidson period these principles were not so obvious. It may be quite possible that local treatment better than tannic acid will be introduced and that better methods of controlling hemocoagulation and infection may be found.

It is not likely, however, that so great an impetus to the advance in the problem will come as that inaugurated by Davidson. At this time, because of warfare, we have need for intelligent treatment of burns. It is appropriate that we pay tribute to the memory of one from this central area who contributed so much to advance our concepts.

UTILIZATION OF PEDICLE SKIN GRAFTS IN CORRECTION OF CICATRICIAL ANAL STENOSIS

WARREN H. COLE, M.D., AND PAUL W. GREELEY, M.D., CHICAGO, ILL.

(From the Department of Surgery, University of Illinois, College of Medicine)

ALTHOUGH in expert hands the results of treatment of imperforate anus in infancy is good, it is true, nevertheless, that in average hands the outcome is poor because of the formation of a stenosing scar at the anus. For the most part the poor results follow incomplete operations in which the rectal pouch is not mobilized sufficiently to bring it down to the skin margin without tension. If there is tension on the suture line between the skin edge and rectal mucosa, the sutures frequently will cut through and the edge of the rectum will retract upward. This leaves a granulating area which produces a stricture after healing. In a few instances this stricture can be controlled by frequent dilatation, that is, two or three times per week for several weeks, and less often thereafter. On other occasions dilatation will be futile.

When the opening is small, incontinence of a liquid type of stool results. The stool becomes liquid through bowel adjustment, otherwise no expulsion of feces whatever would take place. Impaction usually is present and can be felt as large, soft, compressible masses in the abdomen; peristaltic waves are likewise common. Fistula into the urethra (in males) or vagina is common; less frequently, fistulas develop in the perineum adjacent to the anal opening.

When the opening contracts down to a match-head size, as is apt to happen in imperfectly performed operations, or when dilatation has been neglected for the first few years of life, correction then becomes very difficult. In fact, Ladd and Gross¹ remark that when this condition develops, resulting perhaps from a separation at the suture line, the resultant strictured zone "is almost impossible to cure by any subsequent operative procedure." In general, the success of dilatation varies in an inverse ratio with the age of the child, that is, it is more effective in infancy.

It occurred to us that failure in the average operation for neglected stenosis of the anus was due to the fact that there was so much scar tissue that the amount of skin was insufficient at the point of repair. Numerous types of operations have been utilized in an attempt to correct this condition. They are all of the plastic type. The more common ones consist of excision of the scar with undermining of skin flaps, or excision of the scar and mobilization of the terminal end of the rectal

¹Presented at the Second Annual Meeting of the Central Surgical Association, Chicago, Ill., Feb. 27 and 28, 1912.

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sufficient subcutaneous fat in order to have viability insured. It is safer to have previously elevated and delayed this flap so that when it is transferred its circulation will be certain. At the next operation, two or three weeks later, an incision (see Fig. 1) is made from the stenosed anus posteriorly and upward to the rectal mucosa. This opening is dilated, leaving a V-shaped defect. The flap is then mobilized, is transferred to the anal defect, and secured to the cut edges of the mucosa (see Fig. 3). A plug of three per cent xeroform vaseline gauze is then placed in the rectum to exert a moderate amount of pressure against the end of the flap to guard against passive congestion. The donor site is temporarily covered with xeroform vaseline gauze and dry dressings. The wounds are dressed sufficiently often to insure surgical cleanliness and the flap is permitted to remain in this position for three weeks. The silk sutures either cut through and are extruded spontaneously or may be removed in approximately ten days.

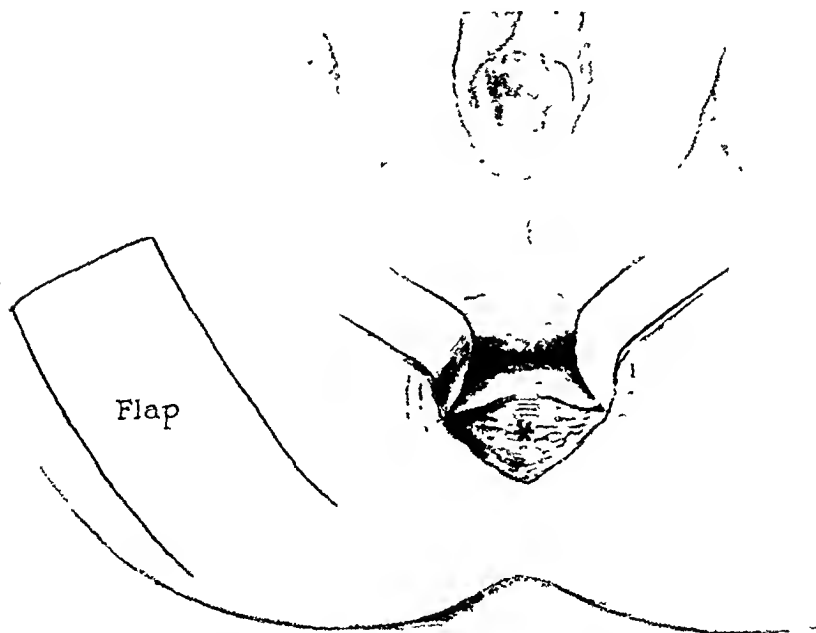


Fig. 2—Two or three weeks after outlining a flap on the buttock, as illustrated, a second operation is performed in which the scar tissue at the stenosed anal opening is cut through posteriorly and the area dilated to make room for the skin graft, as shown in Fig. 3.

At the termination of three weeks the flap is divided and the free end of the distal portion is sutured to the skin at the anal outlet (see Fig. 4). The unused part of the flap (Fig. 4b) is then returned to the donor site and secured in place with interrupted cotton or silk sutures. The balance of the donor site (Fig. 4a) is permitted to fill in by secondary intention although a split skin graft might be applied if the surgeon

wall. On occasions when the stenosis is limited to a very narrow area of tissue, mobilization of the terminal rectum and the use of the Whitehead technique to bring it down, may suffice. A few years ago, Davison² reported the use of prepucce as a skin graft which he transplanted to the anus in an infant to cover the defect after an opening was made into the rectal pouch. Unfortunately, the child died before the final results of the operation could be determined.

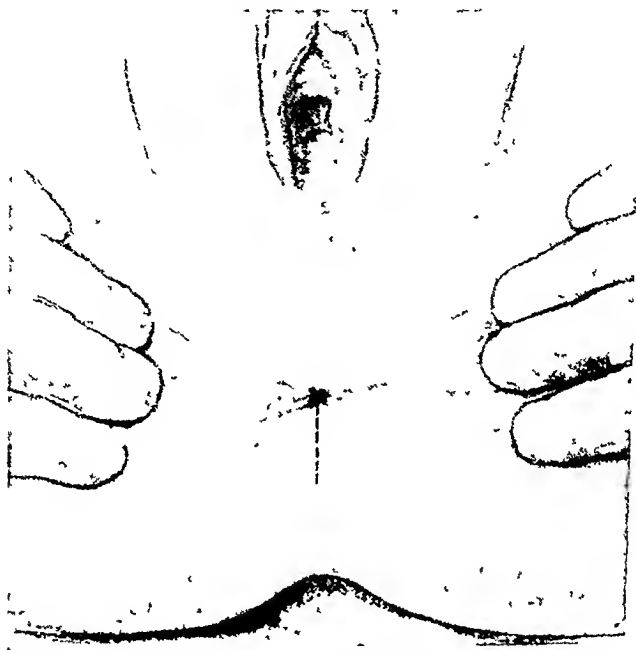


Fig 1—Note the stenosed opening which results from all punctures made for imperforate anus, and many well-performed operations. The dotted line represents the incision made to open the anus, making room for the skin graft, however, there first must be a flap outlined as in Fig 2.

On the assumption that the chief difficulty in the usual type of plastic repair was due to an insufficient quantity of skin or mucosa, we decided to use a skin graft. Since a pedieled graft would have some soft tissue intervening between the grafted skin and the scar, we elected this type of transplant.

As a preliminary step, a temporary colostomy (double-barreled, without tissue intervening) is made in the descending colon so that the anal surgery may be carried out in a clean operative field. After the colostomy is functioning well and the lower loop completely cleaned out by irrigation, the plastic reconstruction of a new anal opening can be started.

About two weeks later, a pedieled flap of skin is elevated from the buttock lateral to the anal opening. This flap is designed so that it will be long enough to reach the anal defect without tension when it is transferred, wide enough to completely cover the defect and contain

However, it appears that the result in one (recent) case may be superior to the first since she is able to retain fairly large quantities of water (200 to 300 c.c.) without spillage.

Our experience with the first case casts doubt upon the amount of peristaltic function which may be regained. For a few weeks the patient had an occasional voluntary stool requiring enemas once or twice a week. However, at the present time (eighteen months after closure of the colostomy) she has no stools except by enema. Whether she has made an improper attempt to develop a normal peristaltic mechanism through her neglect or improper instructions on our part, we cannot say. She has no incontinence whatever unless she has a diarrhea. However, mineral oil taken by mouth tends to leak out her rectum without control, and does not facilitate evacuation. In an attempt to encourage her to develop a normal stool habit we will try mild cathartics, hoping that

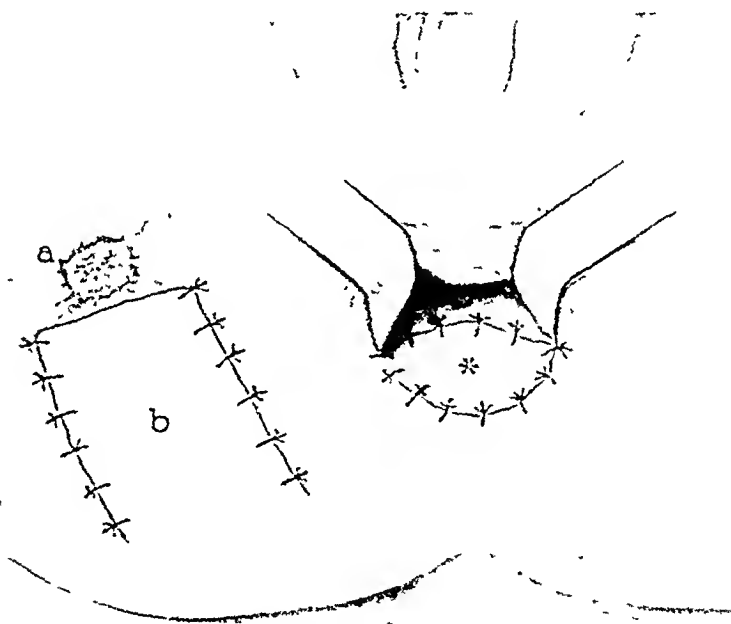


FIG. 4.—Two or three weeks after transplanting the flap to the anal opening the flap is cut transversely, fixing the distal end with sutures to the anal defect and transplanting the proximal portion back to the original site.

from their action, she may learn to develop a stool habit. It seems possible, however, that each patient was obstructed so long that the resultant redundancy of the colon (particularly of the sigmoid), present in each case, may act as a mechanical factor in preventing normal evacuation. In addition to this possibility, it is conceivable that since each had gone for so many years without development of a normal peristaltic mechanism, it might not ever be recovered. This possibility suggests

prefers. The skin sutures are removed within seven to ten days, at which time all of the wounds are healed and the operation at the anus thereby completed. At any time after that, the temporary colostomy is closed by cutting the spur in a Mikulicz fashion and closing the roof at a convenient time thereafter.

The above procedure has introduced a segment of well-vascularized and elastic skin to replace the deficiency at the anal outlet. This will guard against subsequent contraction.

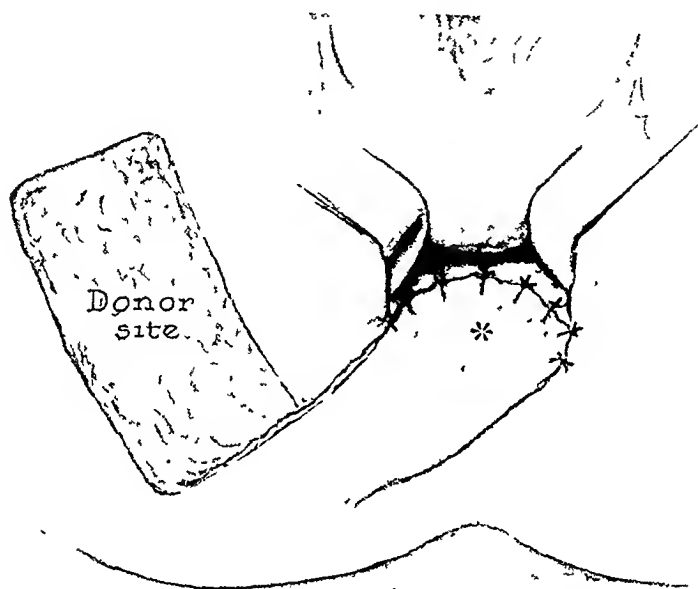


Fig. 3—The skin flap is mobilized and swung over to the midline anchoring the end to the edges of the defect freshly made by the incision posteriorly.

We have operated upon two cases utilizing the above technique with very gratifying results. These two patients were girls, aged 15 and 14 years, each with a history of having been born with an imperforate anus and having incontinence of liquid stools through the stenosed areas which could not be dilated to a size greater than that of a lead pencil. Each had a marked fecal impaction with huge masses palpable at several points in the abdomen and numerous visible peristaltic waves. In each case several days were required to eliminate the impaction. It was interesting to note that in each case there were so few fibers of the anal sphincter left that a definite muscle could not be identified. At first hand, a severe fecal incontinence might be expected, but it is well known that the internal sphincter alone is fairly effective in preventing incontinence, except when the stools are liquid. Neither of our patients has incontinence, although the first has been completed for such a short time (a few weeks) that it is difficult to predict permanent results

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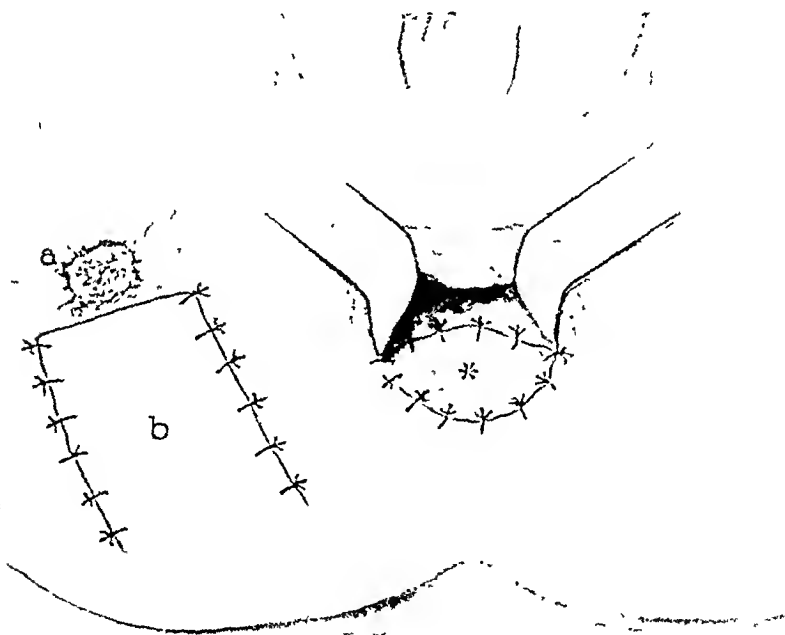


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that operation should be performed at a much earlier date than in our cases. However, we operated on each of our patients shortly after they applied to the dispensary for treatment.

SUMMARY

Patients with imperforate anus frequently develop such a severe stenosis, particularly following inadequate operation at birth, that the ordinary plastic procedure is unsuccessful. In an effort to treat these severe types, we have chosen to use a pedicle skin graft on the assumption that the chief cause of failure in the other plastic procedures was insufficiency in the amount of normal elastic skin.

After doing a preliminary and temporary colostomy of the descending colon, we raised the pedicle flap from the buttock and transferred it into the raw area resulting from correction of the stenosis by incision. We recommend raising the flap at one operation and transplanting it two or three weeks later to insure good blood supply. In each of two cases, transplantation of a flap corrected the stenosis very satisfactorily. Incontinence does not result unless diarrhea is present.

REFERENCES

1. Ladd, W. E., and Gross, R. E.: *Abdominal Surgery of Infancy and Childhood*, Philadelphia, 1941, W. B. Saunders Company.
2. Davison, T. C.: The Use of Prepuce to Epithelialize Tract in the Treatment of Imperforate Anus: *South. Surgeon* 7: 68-70, 1938.

THE EFFECT OF THE TOPICAL APPLICATION OF SEVERAL SUBSTANCES ON THE HEALING OF EXPERIMENTAL CUTANEOUS WOUNDS

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THERE have been many attempts to influence the healing of wounds by the use of medicinal agents. Most of these substances have been prepared for topical application, as ointments, irrigating solutions, or dusting powders. Others have been given orally or parenterally with the idea that the general condition of the organism might favorably affect the reparative process. With the latter method there has been some success; for example, it is generally accepted that vitamin C plays an important part in the formation of new fibrous tissue. On the other hand, although there is a long list of substances which have been recommended for local use to control infection and speed up epithelization in granulating wounds, the surgical literature contains no truly convincing reports.

During a ten-year period beginning in 1916, Alexis Carrel and his associates published a number of papers on the subject of the healing of cutaneous wounds.¹⁻⁴ It was found that noninfected wounds cicatrize according to a regular geometric curve, that the rate of healing is faster in larger wounds, and that wounds in older individuals heal slower. The early latent period was demonstrated, and it was shown that complete absence of irritation caused cessation of healing, while the irritation accompanying minimal infection accelerated healing in Carrel's experiments.

About ten years ago, there was considerable interest in the role of sulfur in wound repair. In an article on the use of thio cresol, Reimann stated,⁵ "The naturally occurring chemical radical SH— which stimulates mitosis has been discovered. Advantage is taken of the chemical group sulphhydryl to stimulate the healing of wounds." Neither of the two wounds described in this communication was entirely healed at the time of the report. Other encouraging clinical reports followed.⁶⁻⁷ Recently, the use of a proprietary containing sulphhydryl has been advocated for the treatment of burns.⁸

Thio cresol was also investigated in an impartial manner by Smelo,⁹ who in 1936 reviewed the literature on the effect of local agents in wound healing and reported the results of his experiments on sixteen patients. He stressed the fact that most clinical studies have been inadequately controlled and the results probably have been assessed incorrectly by enthusiastic writers. He investigated a number of agents during 177

¹Presented at the Second Annual Meeting of the Central Surgical Association, Chicago, Ill., Feb. 27 and 28, 1942.

periods of observation on the sixteen patients with granulating wounds in which there was delayed healing. His list was as follows, (1) admittedly inert agents: petrolatum gauze, physiologic saline solution, and dry gauze dressing; (2) antiseptic agents: merthiolate, merthiolate ointment, mereurochrome, zinc peroxide paste, and a paste consisting of zinc oxide, acaia, and glycerin; (3) presumably stimulating agents: thioeresol in solution and in ointment, irradiated petrolatum, allantoin, peruvian balsam, and ultraviolet radiation. He concluded that the repair process was not significantly altered by any of these agents.

Anderson¹⁰ conducted a similar investigation of the effect of a number of local antiseptics on infected wounds. The following topical agents were used: Dry gauze dressings, moist saline dressings, alcohol dressings, iodoform gauze, azochloramide, merthiolate, eadadyne silver, Dakin's solution, and zinc peroxide cream. He found that these materials had little or no beneficial effect upon the healing of infected wounds, except in the case of zinc peroxide, which favorably affected special cases. These agents did not appear to retard healing by irritation of tissue cells. He suggested that less attention be given to the selection of a local antiseptic agent and more consideration be given to the problem of increasing local tissue immunity and fostering the removal of necrotic tissue by mechanical and chemical débridement.

The possibility that embryonic tissue might contain a hormone or enzyme which would accelerate wound healing has been investigated. Carrel's group used an embryonic tissue extract in their tissue culture experiments,¹¹ but later found that the growing tissue utilized the embryo extract only as a source of nitrogen, and that proteoses obtained by the peptic digestion of fibrin produced a more abundant multiplication of fibroblasts.¹² Satisfactory growth-sustaining proteoses were also obtained from egg white, rabbit brain, and Witte's peptone.

Waugh¹³ investigated an embryonic extract bearing the name of "epitutan," which was made by Albert Fischer of Copenhagen. Four patients were treated for chronic granulating wounds with encouraging results. It is obvious that such a series is too small from which to draw conclusions with regard to wound healing.

The experiments reported in this paper were undertaken at the suggestion of Dr. Alexis Carrel and Dr. Roy D. McClure. It was planned to test the effect of several concentrations of a chloramine paste as well as an embryonic material. The latter was never received for study because Dr. Carrel found himself in Occupied France and his associate, who was interested in this particular material, lost his life in a Channel crossing.

Since the experimental method used in the chloramine paste experiments seemed to be simple and effective, a number of other agents were tested. Two of these were "stand-bys" on the surgical dressing earriages and others were substances which have been recommended recently for the treatment of wounds. In all, ten substances were tested: 1

per cent ehloramine paste, 1.5 per cent ehloramine paste, 3 per cent chloramine paste, scarlet red ointment, peruvian balsam, urea crystals, glycerin, 2 per cent peetin solution, commercial vitamins A and D ointment, and ehlorophyll ointment.

EXPERIMENTAL METHOD

The experimental method was essentially that used by Carrel and his associates in their numerous investigations on the healing of eutaneous wounds. Each substance was tested on twelve guinea pigs. Under ether anesthesia, the abdomen was shaved, prepared with an antiseptic solution (hexyl-chloro-m-cresol¹⁴), and two eutaneous defects were made, one being on each side of the midline. The wound on the animal's left side was consistently used as the test wound and the other served as a control. The wounds were approximately the same size and were usually about the size of a dime (Fig. 1). However, in such an experiment, it is unnecessary for the wounds to be exactly the same size, since there is a strong tendency for wounds in the same individual to heal in the same period of time, even if there is difference in size (Carrel's law).

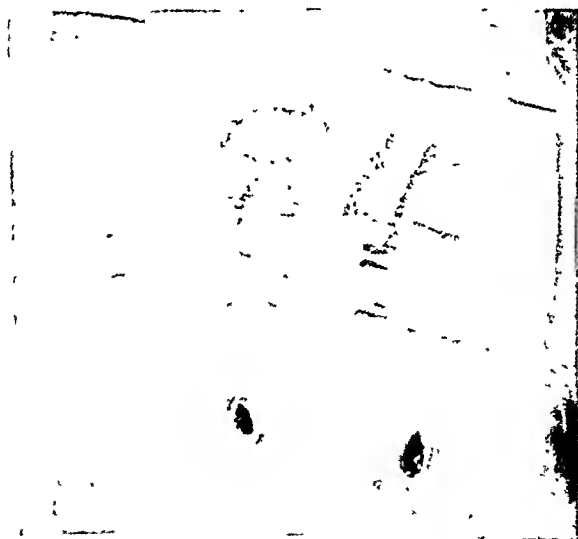


Fig. 1 —Showing the two wounds made on the abdominal wall of guinea pig.

Immediately after the wounds were made, they were outlined on sterile cellophane to record the size, after which the substance to be tested was placed on the appropriate wound. Small sterile gauze dressings were then placed on each wound and held in place by adhesive tape which passed entirely around the animal's body. Such a dressing almost invariably remained in place until the time of the change of dressing. The wounds were dressed every two days, at which time more of the substance to be tested was applied and tracings of the

wound areas were made. The cellophane tracings were transferred to white paper for a permanent record (Fig. 2). In some instances, the areas were computed by means of a planimeter which indicates the areas of irregular figures by a tracing of the perimeter (Fig. 3). From the values thus obtained, graphs of healing could be constructed (Figs. 4, 5, and 6).

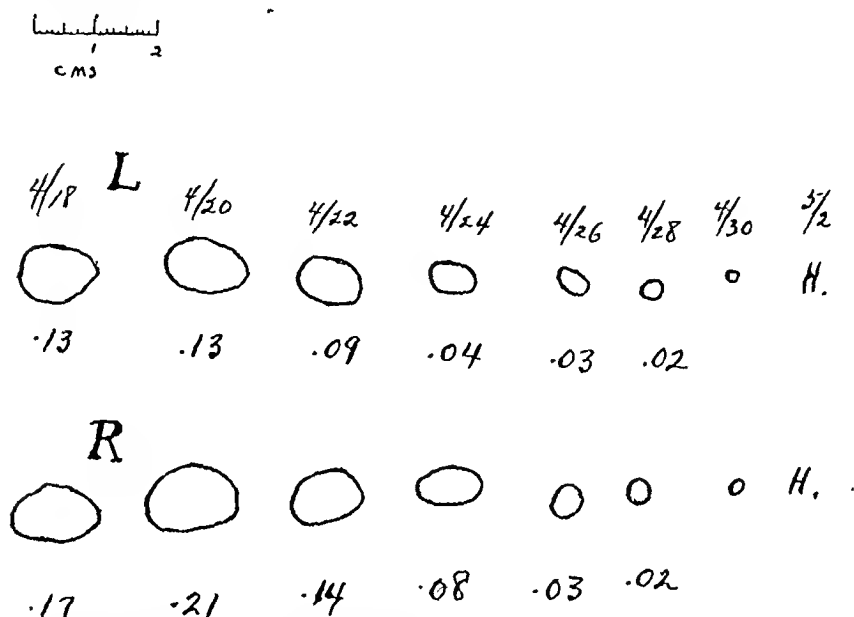


Fig. 2.—Typical record of the healing of wounds in one animal; the left side was treated with glycerin every two days, with no effect on the healing time.

In these experiments, no attempt was made to evaluate the effect of the age of the animals or the nutritional state. They were fed the stock laboratory diet. Presumably each animal served as his own control, although the possibility of absorption from one wound having an effect on the control wound is admitted.

It would serve no useful purpose to present all of the data on the healing of these experimental wounds. A typical experiment on twelve animals is represented in the results obtained when 1 per cent ehloramine paste was applied to the test wound (Table I).

In Table I, it is indicated that healing was apparently accelerated in one animal, unaffected in eight, and delayed in three. It will be noted that where there was a difference in the healing time, it was never more than the two-day dressing period. Actually, therefore, the difference was somewhere between zero and two days. Hence, in evaluating the effect of this ehloramine paste for inclusion in Table II, the summary column indicates that this material had no effect.

TABLE I
1 PER CENT CHLORAMINE PASTE IN TWELVE ANIMALS
(DAYS REQUIRED FOR HEALING)

HEALING	CONTROL WOUND (DAYS)	TEST WOUND (DAYS)
Hastened	14	12
Unchanged	16	16
	16	16
	18	18
	16	16
	12	12
	16	16
	12	12
	16	16
Delayed	16	18
	10	12
	10	12

TABLE II

SHOWING NUMBER OF ANIMALS IN WHICH HEALING WAS HASTENED, UNAFFECTED, OR DELAYED, WITH SUMMARY

MATERIAL TESTED	HASTENED	NO EFFECT	DELAYED	SUMMARY
1% chloramine paste	1	7	3	No effect
1.5% chloramine paste	1	6	5	Delayed (?)
3% chloramine paste	0	4	8	Delayed
Scarlet red	2	8	2	No effect
Peruvian balsam	0	9	3	No effect
Urea crystals	0	0	12	Delayed
Glycerin	1	7	4	No effect
Pectin solution	3	8	1	No effect
Vitamins A and D ointment	3	7	2	No effect
Chlorophyll ointment	4	7	1	No effect

COMMENT ON THE TEN SUBSTANCES TESTED

The experiments show that of the three concentrations of chloramine paste* tried, the 1 per cent variety does not inhibit wound healing, the 1.5 per cent variety has a slight inhibitory effect, while the 3 per cent strength has an appreciable delaying action (eight out of twelve animals).

The chief ingredient in scarlet red ointment is a dye, amino-azotoluene azobetanaphthol. Bettman¹¹ stated, "Scarlet red ointment . . . is definitely stimulating to the epithelium and promotes its growth." The ointment had no effect on the healing of wounds in these experiments. Peruvian balsam is another substance which occupies a place on many surgical dressing carriages. No beneficial effect was demonstrated in this study of noninfected wounds.

A few years ago, there was a wave of enthusiasm for the use of urea solutions in the treatment of open wounds.¹² We have not seen a report of experiments to determine the effect on wound healing. We tried the effect of sprinkling urea crystals on the cutaneous wounds in guinea

*The three chloramine pastes were furnished for investigational purposes by Dr. A. H. Uddin and Dr. L. W. G. Wyckoff of the Lederle Laboratories, Inc.

pigs. The control wounds healed in 10 to 14 days (average 12.3 days) while healing on the treated side was delayed in all animals (Fig. 7). In nine animals, healing was complete in an average of 20.6 days, and in three animals, the wounds were not healed at the end of a thirty-day period. Two of the latter wounds became grossly infected.

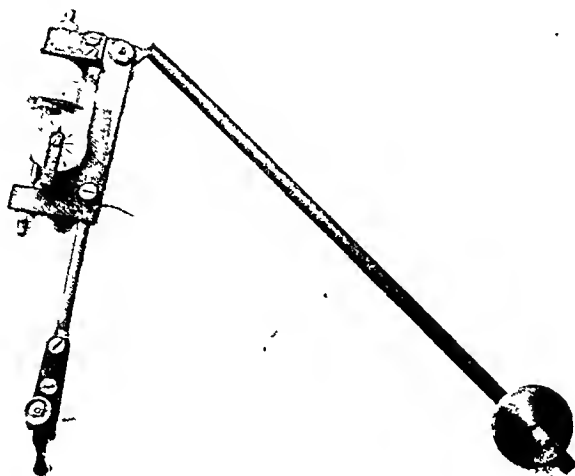


Fig. 3.—Polar planimeter, for determining the area of nongeometric figures. (Instrument purchased from Keufel and Esser, New York.)

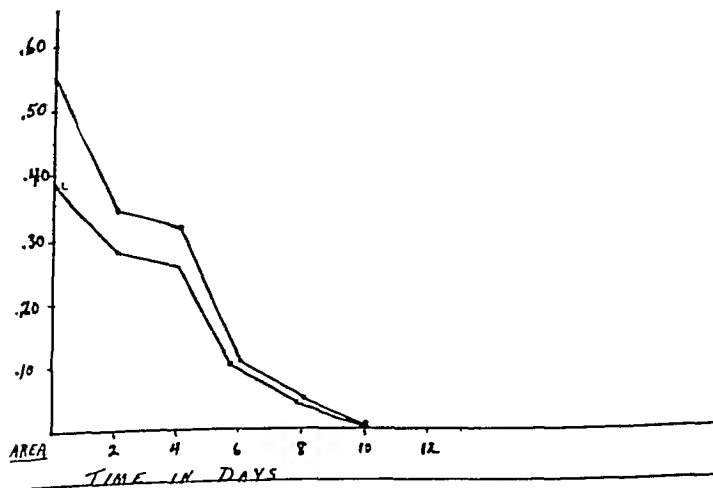


Fig. 4.—Graph of healing of two wounds of unequal size, illustrating Carrel's law that wounds of different size in the same animal tend to heal in the same period of time.

Glycerin has been recommended for topical application to various wounds, including burns, by a number of authors, the latest of whom is Smith.¹⁷ He believed that the osmotic action of glycerin contributed to wound healing by reducing edema through its dehydrating effect. In

our twelve experiments, healing was delayed four times, twice by four days or more, and infection developed in one of the treated wounds.

Tompkins and his associates¹⁸ advised the use of peetin solution for infected wounds. They treated seventy-five cases with chronic wounds, such as decubitus and trophic ulcers, or operative wounds with drainage

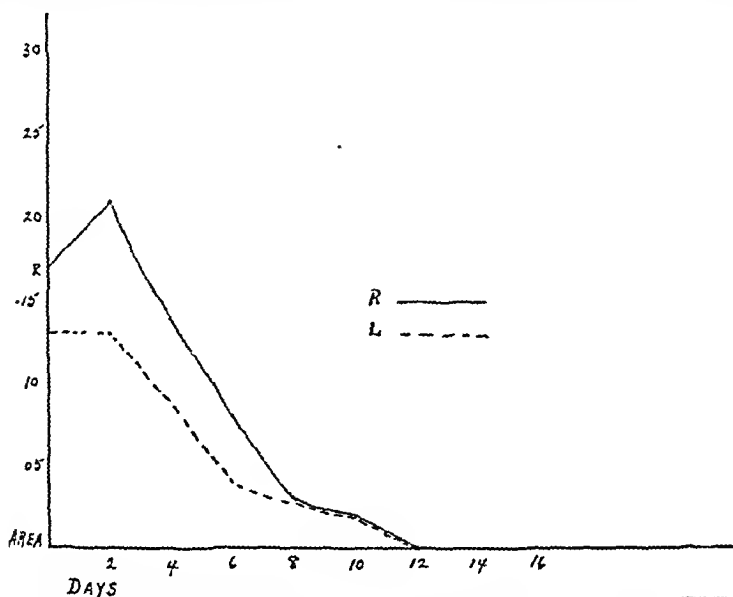


Fig. 5.—Usual result when substances are applied to a wound. no effect; wound on left treated with glycerin.

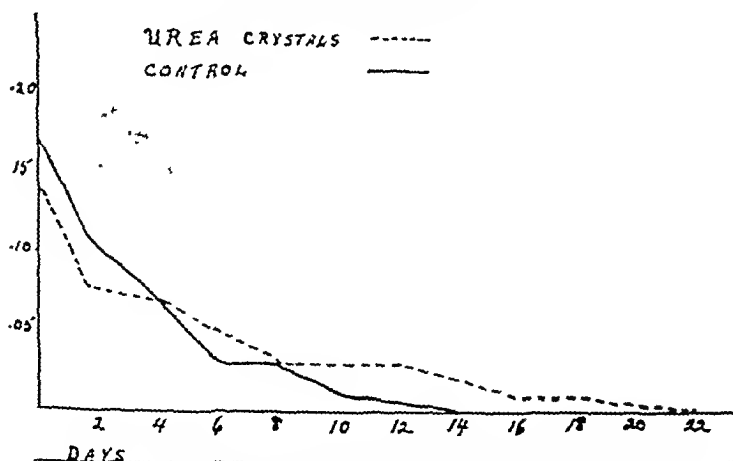


Fig. 6.—Graph of wound healing when urea crystals were applied to the treated wound; healing was delayed eight days.

or secondary infection. They felt that the results exceeded the usual expectations, and emphasized that suppuration seemed to be minimized and that granulation tissue grew abundantly. They made no observations on the effect of peetin on noninfected wounds. In our experiments, peetin had no significant effect on wound healing, although it

pigs. The control wounds healed in 10 to 14 days (average 12.3 days) while healing on the treated side was delayed in all animals (Fig. 7). In nine animals, healing was complete in an average of 20.6 days, and in three animals, the wounds were not healed at the end of a thirty-day period. Two of the latter wounds became grossly infected.

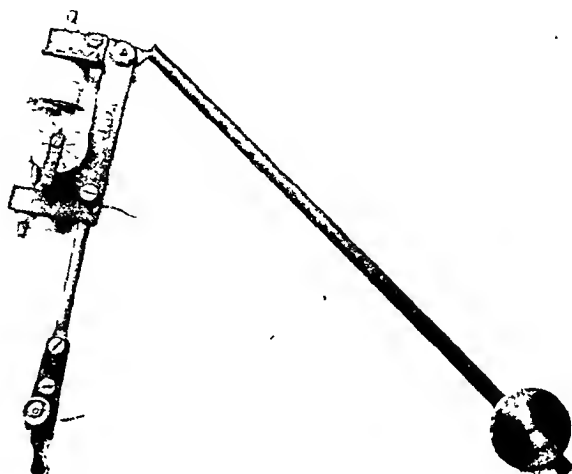


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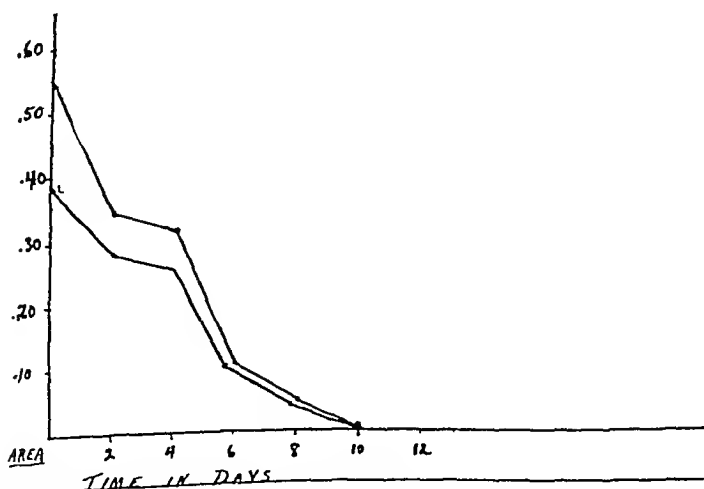


Fig. 4.—Graph of healing of two wounds of unequal size, illustrating Carrel's law that wounds of different size in the same animal tend to heal in the same period of time.

Glycerin has been recommended for topical application to various wounds, including burns, by a number of authors, the latest of whom is Smith.¹⁷ He believed that the osmotic action of glycerin contributed to wound healing by reducing edema.

was prepared. The chlorophyll was presumed to have the formula $C_{55}H_{70}O_6N_4Mg$. In Table II, it is seen that although there was apparent acceleration of healing in four animals, seven showed no effect and in one there was apparent delay. Further experiments using other forms of chlorophyll are planned.

SUMMARY

Ten medicinal agents were applied locally to small wounds in guinea pigs and the healing time compared with control wounds in the same animals. These ten materials were: three concentrations of chloramine paste, scarlet red ointment, peruvian balsam, urea crystals, glycerin, pectin solution, commercial vitamin A and D ointment, and chlorophyll ointment. Of the substances tried, none was found which consistently exerted an accelerating effect on wound healing under the conditions of the experiment. Urea crystals and 3 per cent chloramine paste were definitely inhibitory.

REFERENCES

1. Carrel, A., and Hartman, Alice J.: Cicatrization of Wounds: I. The Relation Between the Size of the Wound and the Rate of Its Cicatrization, *J. Exper. Med.* 24: 429-450, 1916.
2. du Noüy, P. L.: Cicatrization of Wounds: III. The Relation Between the Age of the Patient, the Area of the Wound and the Index of Cicatrization, *J. Exper. Med.* 24: 461-470, 1916.
3. Carrel, A., and du Noüy, P. L.: Cicatrization of Wounds: XI. Latent Period, *J. Exper. Med.* 34: 339-348, 1921.
4. Carrel, A.: Cicatrization of Wounds: XII. Factors Initiating Regeneration, *J. Exper. Med.* 34: 425-434, 1921.
5. Reimann, S. P.: Use and Reasons for the Use of Thiocresol to Stimulate Wound Healing, *J. A. M. A.* 94: 1368-1371, 1930.
6. Birnbaum, I. R.: Thiocresol in Wound Healing and in Skin Grafting, *Ann. Surg.* 96: 467-470, 1932.
7. Brunsting, L. A., and Simonson, D. G.: Cutaneous Ulcers Treated by the Sulphydryl Containing Amino-acid Cysteine, *J. A. M. A.* 101: 1937-1940, 1933.
8. Pierce, W. F.: The Use of Sulphydryl Solution in the Treatment of Burns, *Am. J. Surg.* 53: 434-439, 1941.
9. Smelo, L. S.: The Problem of Wound Healing, *Arch. Surg.* 33: 493-514, 1936.
10. Anderson, D. P.: The Problem of Wound Healing: The Effect of Local Antiseptic Agents on Infected Wounds, *Ann. Surg.* 108: 918-933, 1938.
11. Baker, Lillian E., and Carrel, A.: Action on Fibroblasts of the Protein Fraction of Embryonic Tissue Extract, *J. Exper. Med.* 44: 387-395, 1926.
12. Carrel, A., and Baker, Lillian E.: The Chemical Nature of Substances Required for Cell Multiplication, *J. Exper. Med.* 44: 503-521, 1926.
13. Waugh, W. G.: Experiments in the Acceleration of Wound Healing, *Brit. M. J.* 1: 249, 1940.
14. Hartman, P. W., and Schelling, V.: Antiseptics: Studies on Hexyl-chloro-m-cresol and Other Carbocyclic Antiseptics, *Am. J. Surg.* 46: 460, 1939.
15. Bettman, A. G.: A Simpler Technique for Promoting Epithelization and Protecting Skin Grafts, *J. A. M. A.* 97: 1879-1881, 1931.
16. Muldavin, L. F., and Holtzmann, J. M.: Treatment of Infected Wounds With Urea, *Lancet* 1: 549-551, 1938.
17. Smith, E. D.: Glycerin Osmotic Drainage, *Am. J. Surg.* 50: 55-62, 1940.
18. Tompkins, C. A., Crook, G. W., Haynes, Edith, and Winters, M.: Pectin in the Treatment of Various Types of Wounds, *Surg., Gynec. & Obst.* 72: 222, 1941.
19. Hardin, P. C.: Cod Liver Oil Therapy of Wounds and Burns, *South. Surgeon* 10: 301-338, 1941.
20. Abramowitz, E. W.: Natural Vitamin A and D Ointment, *Indust. Med.* 10: 481-486, 1941.
21. Grushkin, B.: Chlorophyll—Its Therapeutic Place in Acute and Suppurative Diseases: A Preliminary Report of Clinical Use and Rationale, *Am. J. Surg.* 69: 49-55, 1940.

was noted that the granulation tissue appeared more than usually clean and healthy.

There are numerous articles advising the use of vitamin preparations to stimulate epithelization. For example, Hardin¹⁹ stated, "As a wound dressing, it (cod liver oil) possesses a unique stimulating effect on granulation and epithelization. This results in rapid regeneration of tissue defects. The stimulating effect is probably due to its vitamin A and D content . . . it is concluded that commercial ointments are superior to homemade preparations." Abramowitz²⁰ stated, "When applied locally in an ointment base, the natural vitamins A and D stimulate wound healing, especially epithelization." Reference to Table II shows that in our experiments a commercial vitamin A and D ointment* had no effect on the healing time of the noninfected wounds in these presumably healthy animals. It is possible that in the presence of avitaminosis, such a preparation might exert a specific effect.

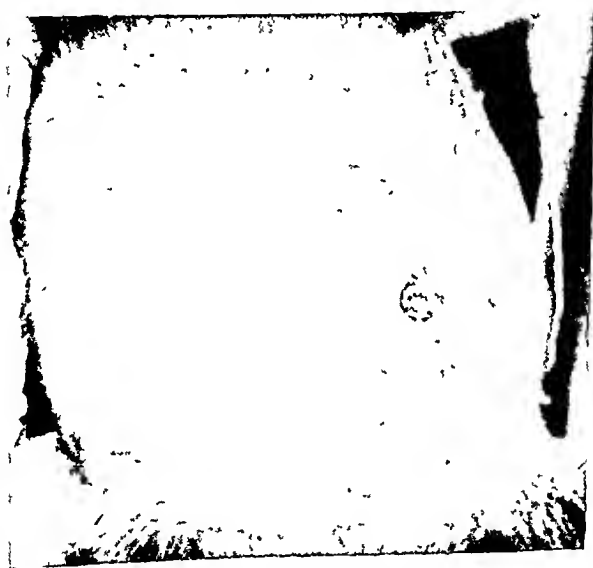


FIG. 7.—Photograph of abdomen of guinea pig showing effect of urea crystals: treated wound on left unhealed, control wound healed, scar hardly visible

Gruskin²¹ reported on the clinical use of chlorophyll in a wide variety of infections, ranging from sinusitis and pyorrhea to subacute bacterial endocarditis. It was hinted that "there is a stimulating effect upon the growth of supportive connective tissue cells and the development of granulation tissue. Similarly, because of this cell activity, it seems logical to believe that there develops an effective barrier to bacterial invasion." It had not been determined whether chlorophyll applied locally would have an effect on epithelization. A chlorophyll ointment consisting of 1 Gm. of oil-soluble chlorophyll† in 25 Gm. of lanolin

*Supplied by the White Laboratories, Inc., Newark, N. J.

†The chlorophyll was obtained from the American Chlorophyll Company through the courtesy of Dr. E. J. Miller of the Experiment Station of Michigan State College.

being one year. His method involved an exposure of Cooper's ligament by retracting the femoral vessels slightly laterally. He then sutured the muscular edge of the internal oblique to Cooper's ligament with four to five heavy silk stitches. Lotheisen refers to this step of the procedure, as follows, "So kommt der schwierigste Akt, das Durchziehen durch das Lig. Cooperi."

The external oblique fascia was then closed over the cord, after which the superficial tissues were brought together.

Fischer (1919).—Stating that he had learned the operation from Kammerer, who was apparently one of the first proponents of the Lotheisen operation in the United States, Fischer stated that he had treated thirty-seven instances of femoral hernia in this manner with no recurrences. In his technique he breaks down Hesselbach's triangle to expose Cooper's ligament. The conjoined tendon is then sutured to the ligament and the external oblique closed over the cord in the manner of a Bassini-McVay operation.

Groves (1923).—This British author used a modified Lotheisen procedure in the treatment of twenty-one cases of femoral hernia during the previous ten-year period. The series included twenty women and one man, the ages varying from 23 to 73 years, and in nine cases the operation was necessitated by strangulation. No recurrences were reported. In his operation, Groves splits Poupert's ligament and then has ready visibility so that the conjoined tendon may be sutured to Cooper's ligament from the pubic spine laterally to the femoral vessels.

Stetten (1923).—This New York surgeon also used the Lotheisen technique through an inguinal incision for femoral hernia. After drawing the femoral sac into the inguinal canal it is inverted and "the typical suture of the edge of the conjoined tendon to Cooper's ligament, covering the iliopectineal line, is made as close to the femoral vein as can be safely done, even angulating it a trifle." He began suturing this layer at the medial angle, but advised against tying the sutures, "of which three or four are needed, until all are placed, as otherwise one has difficulty in placing the most lateral suture next to the vein." We can agree with these statements most heartily, but believe that the difficulty can best be overcome by placing the most lateral suture first.

Andrews (1924).—Working in Chicago, Andrews used the Lotheisen technique to approximate the conjoined tendon and Cooper's ligament with Kangaroo tendon in one case of large femoral hernia.

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CLINICAL EXPERIENCES WITH THE McVAY HERNIOTOMY

ONE HUNDRED AND THIRTY-ONE PERSONAL CASES

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MOST surgeons treating hernias will agree to the following two premises: (1) The three main types of groin hernia are best treated by different varieties of surgical procedure. (2) In the repair of inguinal hernias at least one layer should be sutured to Poupart's ligament.

The present paper offers a technique that defies both of these precepts. An identical technique is used for all of the groin hernias and no layer is sutured to Poupart's ligament.

The field of hernial surgery is receiving increased attention of late because of the necessities of military and industrial fitness during the present national emergency. The number of operative procedures advised for hernial repair indicates the relative inadequacy of most of them in preventing recurrences. This paper discusses the use of a method of repair advised by Lotheisen (1898), and others, for use in femoral hernias and recently modified by McVay (1938-1941) for use in inguinal hernias as well. The series discussed includes 131 hernias operated upon by the senior author (H.N.H.) or his assistants, during the period April 23, 1940, to August 31, 1941. Of the 131 hernias, 80 were operated upon by the senior author personally. The method has been used for all types of groin hernias including indirect inguinal, direct inguinal, femoral, and simple incarcerated, strangulated, or recurrent varieties of several of these anatomic types. The method may be called the Lotheisen-McVay, but since the former writer used it essentially for femoral hernias, we prefer to call it simply the McVay repair.

THE LOTHEISEN OPERATION FOR FEMORAL HERNIA

Several writers have discussed the use of a closure for femoral hernias which involves (1) an inguinal approach, and (2) suture of the conjoined tendon or an adjacent structure to Cooper's ligament. The utilization of Cooper's ligament in place of Poupart's ligament is the essential feature of the operation.

Lotheisen (1898).—This author cited unpublished experiences of Narath with this procedure which he himself first used in a case of recurrent inguinal hernia. Lotheisen used the technique in twelve cases of femoral hernia with no recurrences, the longest period of observation

being one year. His method involved an exposure of Cooper's ligament by retracting the femoral vessels slightly laterally. He then sutured the muscular edge of the internal oblique to Cooper's ligament with four to five heavy silk stitches. Lotheisen refers to this step of the procedure, as follows, "So kommt der schwierigste Akt, das Durchziehen durch das Lig. Cooperi."

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muscular, not aponeurotic, comes down without much tension," whereas we never sew red muscle and use only fascia. In a six-year period, 125 cases at St. Bartholomew's Hospital were treated by suturing this muscular edge to Cooper's ligament, with only three known recurrences. In twenty-one additional cases, Keynes turned down a rather large semicircular flap from the internal oblique layer of the rectus sheath. This was turned at an angle of almost 270 degrees and sutured to Cooper's ligament from the pubic spine as far laterally as the femoral vessels. Speaking of the application of this second modified method to femoral hernia, Keynes stated, "I believe it to be theoretically the best operation for all cases," but practically, in simple cases he merely sutured the internal oblique muscle itself to Cooper's ligament. Fitzmaurice-Kelly (1927), in a letter, opposed Keynes' ideas and preferred a Moscheowitz type of procedure.

Dickson (1936).—Stating that "of all the operations previously proposed for the closure of femoral hernia, the Lotheisen technique comes the nearest to fulfilling the requirements of the anatomical and surgical principles involved," Dickson used a modification of the operation. In his own method he sutured only the transversalis fascia rather than the entire conjoined tendon to Cooper's ligament. Dickson used this operation for femoral hernia only.

McVay (1938 to 1941).—As a result of his anatomic dissections performed at Northwestern University with Anson (1938 to 1940), this author (1939) pointed out that while practically all hernial repairs are based on the theory that the internal oblique and transversalis fibers normally insert into the inguinal ligament, this is not really true. He concluded: "The lowermost fibers of the internal oblique and transversus abdominis muscles do not attach to the inguinal ligament, but insert into the fibrous covering of the pubic pecten, the ligamentum pubicum superius (ligament of Cooper)." McVay advised, therefore, suturing of the inferior aponeuroses of the transversus abdominis and internal oblique to Cooper's ligament. While McVay was not the first to describe this operation, most previous writers used it only in the repair of femoral hernias. McVay broadened its use and by a careful dissection of the inguinal region of over 300 cadavers, has placed the operation on a sound scientific basis. This is our reason for referring to the procedure as the McVay herniotomy.

Goinard (1939).—This French writer used the technique for inguinal hernias. During the three years preceding his report he treated fifteen inguinal hernias, six of them recurrent, by suturing the conjoined tendon to Cooper's ligament. Goinard called attention to the solidity of the repair as determined by palpation in the wound after the deep layer of sutures had been placed.

McClure and Fallis (1939).—These authors also used the Lotheisen type of repair in about one-third of their series of ninety femoral hernias.

Amendola (1941).—In an unpublished report, this author stated that he occasionally sutured the transversalis fascia to Cooper's ligament for repair of inguinal hernias.

Neuhof (1942).—In a recently published report, this author made the same recommendation as Amendola (1941).

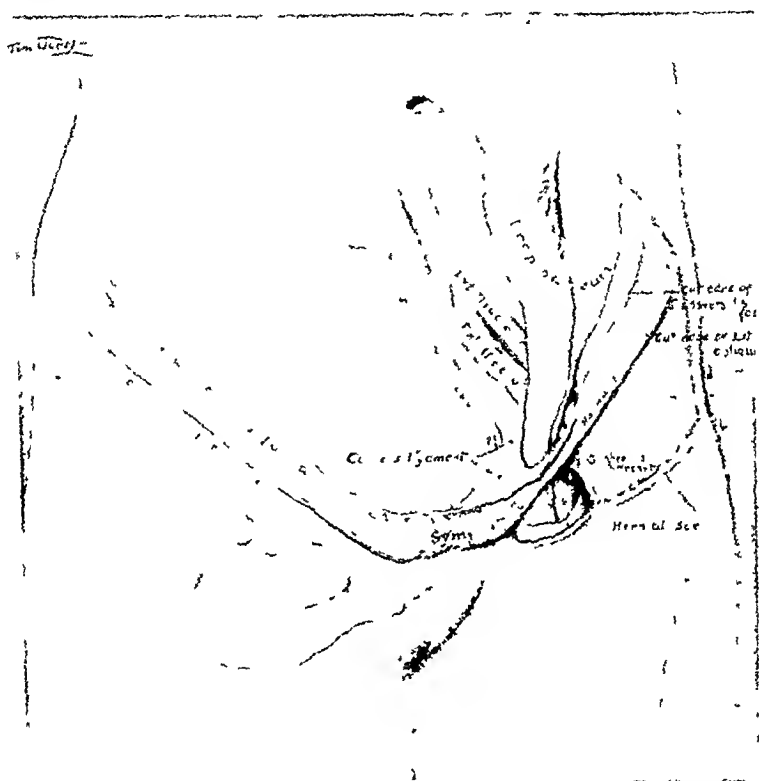


Fig. 1—Dissection of female pelvis to show Cooper's ligament in case of femoral hernia (From Seelig and Tuholske Surg., Gynec & Obst 18, 57, 1914)

COOPER'S LIGAMENT (LIGAMENTUM PUBICUM SUPERIUS)

Fig. 1 is taken from the article of Seelig and Tuholske (1914) and represents a special dissection which they made to correct the previous lack of knowledge concerning Cooper's ligament. They stated, "It is equally unfortunate that probably the most important structure utilized in the closure of the femoral ring, namely, Cooper's ligament, is not only not pictured in any of the anatomies, but also is not adequately described in most of them." Cooper's ligament was first described by Sir Astley Cooper (1804) when he cited the os pubis as being "covered by a ligamentous expansion, which forms a remarkably strong production above the linea iliopectinea, extending from the tuberosity of the pubis outward, and projecting from the bone over that line."

Seelig and Tuholske pointed out the inadequacy of even this classical definition. Briefly, the fascial bundle at the upper edge of the ramus of the pubis is Cooper's ligament.

TECHNIQUE

General Principles.—In general, we prefer not to do elective herniotomies in the winter months, but do not make this a hard and fast rule. Spinal anesthesia, silk technique with interrupted sutures throughout (except for purse-string sutures), skin preparation with 3.5 per cent iodine, and return to manual labor in from five to six weeks after operation are elements in the procedure. The use of silk is justified by the fact that there was not a single instance in the entire series of 131 McVay herniotomies in which any subcutaneous silk was extruded. The technique may be divided into ten steps. The time required for the operation is no greater than for a conventional repair.

1. *Exposure of the cord and opening of the indirect sac.* A skin incision is made from 1 cm. medial to the anterosuperior iliac spine to over the pubic spine exposing the external oblique aponeurosis. The external ring is exposed and the external oblique aponeurosis split in the direction of its fibers even with the upper border of the ring. This splitting is best begun 3 cm. from the ring with the knife. The split is then extended laterally and upward with scissors, and then more carefully downward in the direction of the external ring after meticulously peeling away the ilio-inguinal nerve which is often adherent to the under surface of the external oblique aponeurosis. When it is cut, this accident usually occurs near the external ring and may be prevented by approaching the latter from the lateral side. The cord and surrounding structures are then separated from the lower leaf of the external oblique aponeurosis and Poupart's ligament, then from the region of the pubic spine and conjoined tendon so that finally the cord is freed entirely except at both ends. The indirect sac, which is always present even in normal individuals, is located upward and medialward from the internal ring and is then opened not only in indirect and combined types of hernias, but also in simple direct or femoral hernias. If the indirect sac is long it is bisected, after careful separation from the cord, near the internal ring. The distal segment is usually left undisturbed and rarely causes trouble, but if easily separated, is removed. The proximal segment is grasped with Halsted clamps at points around the circumference of the internal ring.

2. *Exploration.* The large number of small femoral or direct hernias that "recur" after an indirect inguinal herniotomy is in many instances testimony against the inaccuracy of the diagnosis, rather than the incompetency of the procedure. It is indeed surprising how few surgeons will place an index finger into the abdomen through an indirect sac for purposes of exploration of the femoral ring and Hesselbach's triangle,

even though the sac lies open before them. We believe that this is an essential feature of all herniotomy repairs.

3. *Hoguet maneuver.* If a direct weakness or sac exists, we then transpose it laterally to the inferior epigastric vessels by the technique of Hoguet (1920), which has since been popularized by Fallis (1938). Thus, the direct and indirect sacs are converted into one. This step may be described in Hoguet's own words, as follows, "By traction outward on the indirect sac, all of the peritoneum of the direct sac may be pulled external to the vessels and the two sacs converted into one. An indirect sac can always be found in these cases, although it may be very small." The same procedure may be used to convert a femoral sac into an indirect sac, as used by McClure and Fallis (1939). In some instances, all three sacs may be converted into a single indirect sac which can always be dealt with as described in Step 4.

4. *Internal purse-string closure of indirect sac.* The indirect sac, whether it be simple or enlarged by the conversion of direct and femoral sacs, is then closed with an internal purse-string suture of No. 5 heavy silk. Many bites are taken so as to include all crevices and the suture is placed with a round noncutting needle as high as possible.

5. *Plastic on the internal ring.* When the purse-string suture is cut and the peritoneum snaps back, the defect in the transversalis fascia at the internal ring is seen to be quite large in many instances. The fascia is grasped with Allis clamps at numerous points around the internal ring above and medially as far as the inferior epigastric vessels but not inferior to the cord and a second purse-string suture of heavy silk placed in the transversalis fascia. This makes a snug fit around the cord. (The purse string itself does not surround the cord.)

6. *Relaxation of the internal oblique.* The inner layer of the anterior rectus fascia is routinely split for a distance of about three inches from a point $1\frac{1}{2}$ cm. above the pubic spine upward and lateralward. This is done almost exactly as described by Rienhoff (1940) and as shown in Figs. 2 and 3. The external oblique is lifted up by the assistant and the internal oblique cut just lateral to the junction of the two to form the linea alba. The rectus and pyramidalis muscles are exposed. The iliohypogastric and adjoining nerves and vessels which enter the rectus muscle through the internal oblique aponeurosis at this point can be avoided easily. This relaxation allows the internal oblique and attached transversalis fascias to be pulled down for the subsequent repair without tension.

7. *McVay sutures.* The "red" muscle of the internal oblique is entirely disregarded and even may be excised for convenience where it overlies the conjoined tendon. Usually it is elevated with a small retractor and the conjoined tendon located with a gauze (Küttner) dissector. If the transversalis fascia alone appears strong enough, it alone is used for the upper leaf of the repair. If it is not adequate, one must go higher and include the internal oblique aponeurosis. In

no case, however, should "red" muscle be used. The lower leaf is Cooper's ligament. The left index finger is placed on the anterior ramus of the pubis near the spine and moved laterally along the crest until the femoral vessels are reached. This is usually about 5 cm. lateral to the spine of the pubis. Since the finger is held in close contact with the bone, keeping the vessels lateral, and the first stitch is

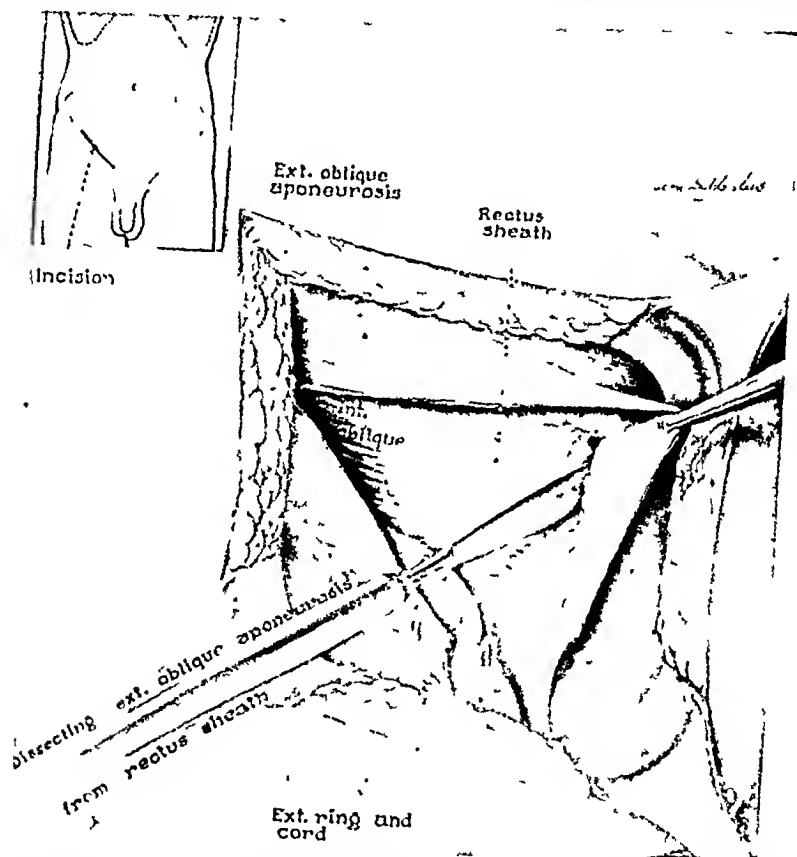


Fig 2—Relaxation of the internal oblique preliminary exposure. We usually do the separation with blunt dissection and then cut through the internal oblique aponeurosis just lateral to where it joins the external oblique aponeurosis to form the linea alba. The iliohypogastric and other nerves and vessels to be avoided are not shown in the above illustration. (From Rienhoff SURGERY 8: 333, 1940.)

placed medial to the finger, there is little danger of damaging the vessels. The first stitch, thus, is usually 4 cm. lateral to the pubic spine. Therefore, since the upper leaf is to be grabbed with the suture first, the needle goes through the transversalis fascia a corresponding distance of about 4 cm. from the pubic spine and then through the thick Cooper's ligament on the upper border of the pubic ramus, locating the ligament by feeling the bone with the needle. This stitch is then tied and the intervening gap between this point and the pubic spine closed with three or four similar sutures (see Fig. 4). These

sutures are a double strand of No. 5 heavy braided silk and are applied on a round small curved Mayo needle with a Bland needle holder. The double strands are tied three times and then separated and the individual strands tied in pairs. In certain cases, because of the presence of a lymph gland or doubt as to the position of the vein, the sutures are carried out only about halfway from the pubic spine to the femoral vessels. This procedure, which we call a "partial McVay," was done only once by the senior author (H. N. H.) but fifteen

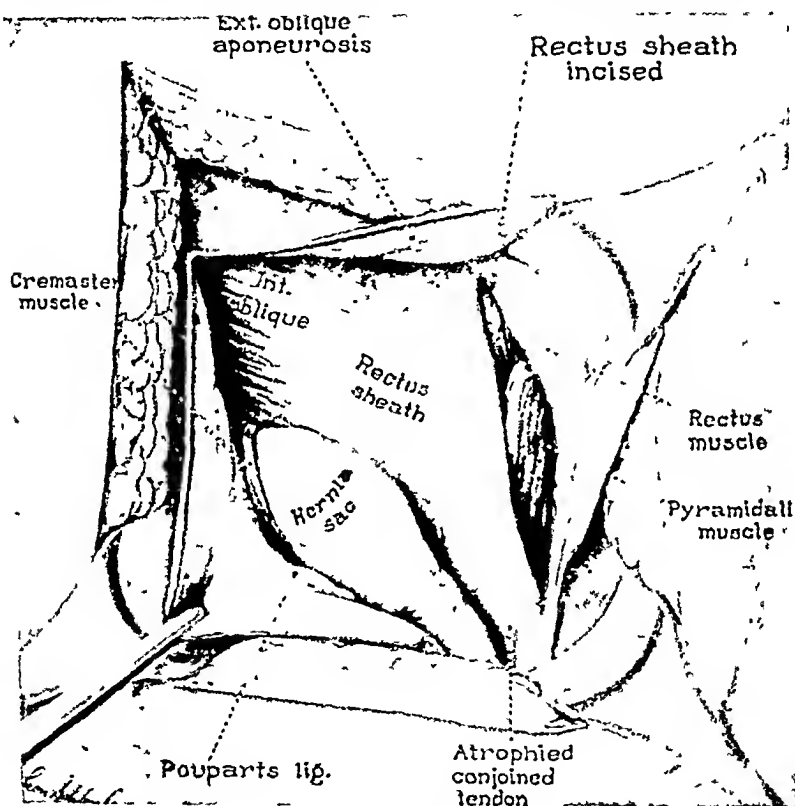


FIG 3—Relaxation of the internal oblique result (From Rienhoff SURGERY 8: 334, 1940)

times by another of us (D. E. S.). In such cases, the transversalis fascia lateral to the McVay closure is fastened to Poupart's ligament. Except for the one case cited above, the senior author depends entirely on the plastic on the internal ring to close the latter, placing no deep sutures lateral to the McVay closure.

8. Closure of the external oblique aponeurosis. In eighty instances this was done beneath the cord after the manner of the original Halsted procedure, while in the remaining fifty-one cases of hernia the cord was dropped into the space left by the McVay closure and the external

oblique aponeurosis closed over it in a typical Bassini manner. Fine No. 1 interrupted silk is used for this and the more superficial layers. These two variations denote what we call the Halsted I-McVay and Bassini-McVay procedures. At first the senior author did all cases by the former, while during the past year he has done all cases but one by the Bassini-McVay procedure. There have been no recurrences by the latter method and one by the former.

9. *Closure of Scarpa's fascia.* Closure of Scarpa's fascia with small bites of the suture seems more anatomic and leaves less silk than does suture of the fat with large bites taken at random. The sutures are preferably placed so that the knot will be down.

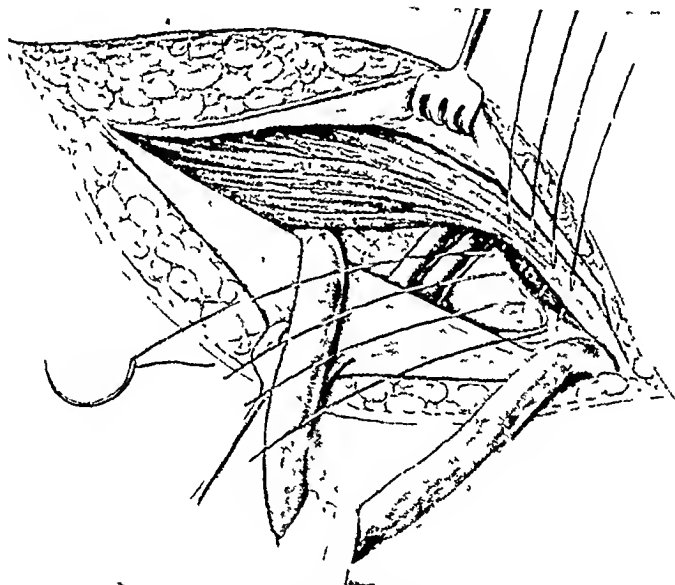


Fig. 4.—Diagrammatic representation of McVay sutures. We reflect the "red muscle" of the internal oblique upward and grasp the underlying transversalis (in some cases internal oblique) aponeuroses for the upper leaf of the repair. We also do not break down Hesselbach's triangle in most cases so that the femoral vessels are not exposed as they are here in this illustration (From Stetten Ann Surg. 78: 57, 1923)

10. *Skin closure.* This is best done with interrupted silk and end-on mattress sutures should be used for at least the lower third of the incision inside the hairline.

MATERIAL

Using the modified McVay or McVay-Lotheisen technique described above, we have repaired 131 groin hernias in 109 patients during the period April 23, 1940, to August 31, 1941. Since August, 1941, the senior author has used this technique for all cases, whereas previously in the period covered by this report only the larger hernias were treated by the McVay method, a simple Bassini or original Halsted

being used for the smaller hernias. Thus, to some extent, the cases analyzed below represent a selected group of difficult hernias and direct hernias.

Sex.—The predominance of males in our series, as shown in Table I, reflects the usual sex difference exaggerated by the industrial character of our clientele.

TABLE I

SEX

	NUMBER OF PATIENTS	PERCENTAGE
Male	107	98
Female	2	2
Total	109	100

Age.—The youngest patient was a boy, aged 7 years, while the oldest was a man, aged 66 years. The ages of over 80 per cent of the patients in the series fall in the third, fourth, and fifth decades, that is, the ages of greatest physical activity, between 21 and 50, as shown in Table II.

TABLE II

AGE

AGE GROUP	DECADE	NUMBER OF HERNIAS	PERCENTAGE
1 to 10	1	1	1
11 to 20	2	5	4
21 to 30	3	12	9
31 to 40	4	26	20
41 to 50	5	43	33
51 to 60	6	41	30
61 to 70	7	3	3

Occupation.—The majority of the patients, as seen in Table III, were engaged in hard labor. Practically invariably patients with unilateral hernias returned to work in five weeks, and those with bilateral and recurrent, in six weeks after operation.

TABLE III

OCCUPATION

	NUMBER OF PATIENTS	PERCENTAGE
Hard labor	86	79
Sedentary	23	21

Side.—The right side was operated upon most often, as shown in Table IV, while in twenty-two instances a bilateral McVay procedure was performed. This table refers to this type of operation only; in several instances other procedures were done on the other side which are not listed. In every such instance the McVay procedure was performed on the side with the largest hernia. For technical reasons a left-sided McVay operation is more difficult to perform than a similar operation on the right side.

TABLE IV

SIDE

	NUMBER OF PATIENTS	PERCENTAGE
Right alone	55	50
Left alone	32	29
Bilateral	22	21

Size of Hernia.—In the total list of 131 hernias, 55 were listed as large (sac 10 cm. or over in its longest diameter), 55 as medium (sac 5 to 10 cm.), and 21 as small (sac less than 5 cm.) (Table V).

TABLE V

SIZE OF HERNIAL SAC

	NUMBER OF HERNIAS	PERCENTAGE
Large	55	42
Medium	55	42
Small	21	16

Classification.—As seen in Table VI, the proportion of the various types of hernia represented is approximately that found in an average series. The one exception to this statement is the large number of patients with direct inguinal weakness. This is partly because early in the series, when the McVay procedure was still viewed somewhat as an experimental trial, it was used especially for direct hernias. Later, however, it was used in all cases and during the past six months the senior author (H. N. H.) has used no other type of repair. Another reason for the large number of direct hernias is that with routine inspection of Hesselbach's triangle with the gloved index finger from inside, we detect a large number of direct weaknesses that would otherwise go unnoticed.

TABLE VI

TYPES OF HERNIA REPRESENTED

CLASSIFICATION	NUMBER	PERCENTAGE
Simple indirect	40	30
Simple direct	34	26
Indirect + direct (saddlebag)	31	23
Femoral + indirect	5	4
Femoral + saddlebag	2	2
Sliding	1	1
Recurrent direct	9	7
Recurrent indirect	9	7

Duration.—Because of increased surveillance of industrial workers, most of the hernias were operated upon early. Approximately 50 per cent were treated within six months of the onset of symptoms (Table VII). In many instances, however, where a short history was claimed, a congenital type of sac was found, indicating a longer duration.

Anesthesia.—Most of the patients (93, or 85 per cent) received spinal anesthesia (spinocaine) as shown in Table VIII. The better relaxation

TABLE VII

DURATION

	NUMBER OF HERNIAS	PERCENTAGE
1 day to 1 week	1	1
1 week to 1 month	25	19
1 month to 6 months	40	31
6 months to 1 year	12	9
1 year to 5 years	23	18
More than 5 years	21	16
Unknown or congenital	9	6

produced by this method permits a much more accurate anatomic dissection. Its only disadvantage is that the tissues are so loose that one is tempted to imbricate more than the actual tension of the muscles after the cessation of anesthesia will permit.

TABLE VIII

ANESTHETIC

	NUMBER OF PATIENTS	PERCENTAGE
Spinal	93	85
Ethylene-ether	12	11
Local	4	4

Type of Operation.—As shown in Table IX, most of the hernias, 69 in number, were treated by the Halsted I-McVay technique, and 46 by the Bassini-McVay technique (external oblique aponeurosis under or over the cord respectively). The senior author (H. N. H.) has switched over almost entirely to the Bassini-McVay technique during the past year. Of the 16 partial McVay operations, only one was done by the senior author.

TABLE IX

TYPE OF OPERATION

	NUMBER OF HERNIAS	PERCENTAGE
Bassini-McVay	46	35
Halsted I-McVay	69	53
Partial Bassini-McVay	5	4
Partial Halsted I-McVay	11	8

Follow-Up.—This paper includes in no sense a complete follow-up and the longest period of observation in any instance is twenty-one months. Only one recurrence was observed, occurring in a case operated upon fourteen months before using a Halsted I-McVay type of repair. This operation was done by one of the younger assistants. The recurrence was in a sac, 2 cm. in diameter, occurring over the internal ring which probably had not been made snug enough. Since in Fallis' series of 800 hernias, the recurrence rate at the end of one year was already 4.2 per cent (despite the ultimate maximum of only 8.5 per cent), this indicates that our series is at least no worse than other series with a good result. However, we wish to draw no pre-

mature conclusions in this regard and a study of the recurrence rate is not the prime purpose of our report.

Complications.—As seen in Table X, wound infections and other local complications were nonexistent, even using the strictest meaning of the terms. This result is attributable, we believe, to the use of silk in all cases including strangulated hernias. The senior author (H. N. II.) and his assistants have performed 360 groin herniotomies during the past two years, using silk in every case, and in only one instance did buried silk have to be pulled out of the wound; this case was not a McVay operation and in it the extrusion of silk was completed in less than eight weeks and the hernia did not recur. The incidence of post-operative pain was somewhat high, but was temporary in many instances and was no higher than in our other cases where the McVay technique was not used. The factor of compensation may have played a role in some cases. The one instance of swelling of the ankle aroused some doubt as to the danger of compressing the femoral vein. The extreme localization of the swelling to the ankle casts doubt on this fear as does the fact that in Fallis' series of conventional herniotomies, phlebitis occurred in 0.18 per cent of the cases. Swelling of the testicle also did not occur in an unusual number of our cases and tended to improve.

TABLE X
COMPLICATIONS

	NUMBER OF HERNIAS	PERCENTAGE
Hematomas, wound infections, silkosis	0	0
Pulmonary complications	0	0
Edema of ankle	1	1
Swelling of testicle	2	2
Postoperative pain	18	14
Recurrence	1	1

SUMMARY AND CONCLUSIONS

1. Based on the theory that the transversalis and internal oblique fibers do not normally attach themselves to Poupart's, but rather to Cooper's ligament, a hernial repair has been utilized which attempts to restore the normal attachments to Cooper's ligament. In this operation, termed the McVay herniotomy, no fascial layer is sutured to Poupart's ligament.

2. This technique has been used in the repair of 131 groin hernias of several types in 109 patients during a sixteen-month period. While the follow-up studies are not yet complete, the results indicate that the procedure justifies its theoretical advantages. To date only one recurrence has been found.

3. An identical procedure is used for all of the main types of groin hernias, indirect inguinal, direct inguinal, and femoral. The fact that only one technique need be learned is another advantage of this method.

REFERENCES

1. Amendola, Frederick H.: Repair of Hernia With a Silk Binding-Stitch, paper read before the New York Surgical Society, Oct. 8, 1941.
2. Andrews, E.: The Closure of Large Femoral and Inguinofemoral Defects the Result of Relaxation of Poupart's Ligament, *Surg., Gynec. & Obst.* 39: 754-759, 1924.
3. Anson, B. J., and McVay, C. B.: Inguinal Hernia. I. The Anatomy of the Region, *Surg., Gynec. & Obst.* 66: 186-191, 1938.
4. Cooper, Sir Astley (1804): Cited by Seelig and Tuholske, 1914.
5. Dickson, A. R.: Femoral Hernia, *Surg., Gynec. & Obst.* 63: 665-669, 1936.
6. Fallis, L. S.: Inguinal Hernia: A Report of 1,600 Operations, *Ann. Surg.* 104: 403-418, 1936.
7. Fallis, L. S.: Direct Inguinal Hernia, *Ann. Surg.* 107: 572-581, 1938.
8. Fischer, Hermann: Lotheisen's Operation for Femoral Hernia, *Ann. Surg.* 69: 432-434, 1919.
9. Fitzmaurice-Kelly, M.: The Modern Treatment of Hernia, *Brit. M. J.* 1: 491-492, 1927.
10. Goinard, P.: Cure radicale de certaines hernies inguinales par fixation du tendon conjoint au ligament de Cooper, *Presse méd.* 47: 872, 1939.
11. Groves, E. W. Hey: A Note on the Operation for the Radical Cure of Femoral Hernia, *Brit. J. Surg.* 10: 529-531, 1923.
12. Hoguet, J. P.: Direct Inguinal Hernia, *Ann. Surg.* 72: 671-674, 1920.
13. Henry, A. K.: Operation for Femoral Hernia by a Midline Extraperitoneal Approach: With a Preliminary Note on the Use of This Route for Reducible Inguinal Hernia, *Lancet* 1: 531-533, 1936.
14. Iason, A. H.: Hernia, Philadelphia, 1941, The Blakiston Company.
15. Keynes, Geoffrey: The Modern Treatment of Hernia, *Brit. M. J.* 1: 173-179, 1927.
16. Keynes, G.: The Modern Treatment of Hernia, *Brit. M. J.* 1: 595-596, 1927.
17. Lotheisen, George: Zur Radikaloperation der Schenkelhernien, *Centralbl. f. Chir.* 25: 548-550, 1898.
18. McClure, R. D., and Fallis, L. S.: Femoral Hernia: Report of Ninety Operations, *Ann. Surg.* 109: 987-1000, 1939.
19. McVay, C. B., and Anson, B. J.: Aponeurotic and Fascial Continuities in the Abdomen, Pelvis and Thigh, *Anat. Rec.* 76: 213-231, 1940.
20. McVay, C. B., and Anson, B. J.: Composition of the Rectus Sheath, *Anat. Rec.* 77: 213-225, 1940.
21. McVay, C. B.: An Anatomic Error in Current Methods of Inguinal Herniorrhaphy, *Ann. Surg.* 113: 1111-1112, 1941.
22. Neuhof, H.: An Operation for Inguinal Hernia Based Upon the Utilization of Cooper's Ligament, paper read before the New York Surgical Society, Oct. 8, 1941.
23. Rienhoff, W. F.: The Use of the Rectus Fascia for Closure of the Lower or Critical Angle of the Wound in the Repair of Inguinal Hernia, *SURGERY* 8: 326-339, 1940.
24. Seelig, M. G., and Tuholske, L.: The Inguinal Route Operation for Femoral Hernia; With a Supplementary Note on Cooper's Ligament, *Surg., Gynec. & Obst.* 18: 55-62, 1914.
25. Stetten, DeW.: Further Observations on a Modified Inguinal Hernioplasty Technique, With Completed Utilization of the Aponeurosis of the External Oblique, *Ann. Surg.* 78: 48-60, 1923.

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carcinoid tumors at the Johns Hopkins Hospital, a total of twenty-nine cases. He concluded that they are not peculiar to any age group, since his youngest patient was 12 and the oldest 66 years of age. The average age was 35 years; however, he noted that carcinoid tumors of the appendix appeared at an earlier age than those of the small intestine and colon. The stomach tumor was found in a man of 55 years. In his series, all of the carcinoids of the stomach and large intestine were malignant. The majority of those of the small intestine and appendix were benign.

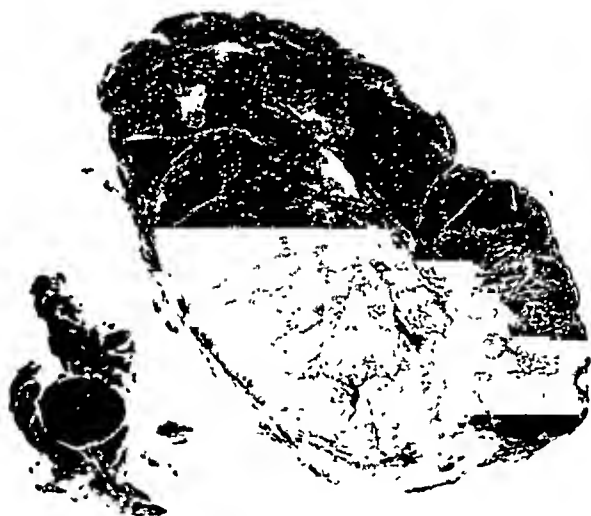


Fig. 1.—Gross specimen of tumor (metric measurement).

V. Pettinari⁷ of Lombardi, Italy, reported the first successful removal of a carcinoid tumor of the stomach. This was in 1935. His patient was a male, aged 47 years, who had had complete pyloric obstruction.

Entwistle,⁸ in 1937, successfully removed multiple carcinoid tumors from the stomach of a young woman, 25 years of age. She complained of moderately severe abdominal pain accompanied by nausea, vomiting, and a massive hematemesis. Blood transfusions and conservative treatment improved her condition so that roentgenographic examination was deemed safe; this revealed punched out areas suggestive of multiple polyposis. Exploration revealed six firm tumors of the gastric wall which were excised. Operation completely relieved the patient of her symptoms.

CASE REPORT

Mrs. A. H. was a white woman, aged 14 years, whose occupation was nursing. Her chief complaint was "bloody stools." In February, 1925, she complained of

CARCINOID TUMORS OF THE STOMACH

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(From the Department of Surgery, University of Wisconsin, School of Medicine)

CARCINOID tumors were first described by Langhans, in 1867. He described a polypoid tumor involving the submucosa and muscularis of the ileum which presented an alveolar and infiltrating structure, now clearly recognizable as that of the typical carcinoid.¹ In 1888, Lubarsch clearly distinguished between carcinoids and ordinary adenocarcinoma. In 1904, Bunting noted the structural resemblance to basal cell carcinoma and in 1907, Oberndorfer employed the term "carcinoid."² Gosset and Masson first demonstrated the affinity of certain granules in the cytoplasm of the cells for silver salts and called these argentaffin cells and the tumor argentaffinoma.³

This type of tumor is most frequently found in the appendix, less commonly in the intestine and colon, and infrequently in the stomach. Humphrys analyzed 152 cases of intestinal carcinoids and found that in 30 per cent the tumors were multiple; and, in addition, in 16 per cent there were metastases to the mesenteric lymph nodes.³ In our series of thirty-one cases the tumors were located as shown in Table I.

TABLE I
CARCINOID TUMORS

LOCATION	NUMBER OF CASES	NUMBER MALIGNANT	PER CENT MALIGNANT
Appendix	26	2	7.7
Small intestine	3	2	66.7
Liver (metastatic)	1	1	100.0
Stomach	1	0	0.0
Totals	31	5	17.5

The total malignancies were 17.5 per cent. This is in accord with Ritchie's figure of 20 per cent showing malignancy.

In 1939, Plaut,⁴ in reviewing the literature, was able to collect only nine cases of carcinoid tumors of the stomach and of these only three gave clinical signs and symptoms which resulted in operation and diagnosis. One other, reported by Walley,⁵ was discovered on gastroscopic examination and successfully removed. The remaining five cases were discovered at autopsy. He reports one additional case found in a routine necropsy.

In 1933, Raiford⁶ reported the first clinical case of a carcinoid tumor of the stomach. An exploratory celiotomy was done and metastases to the lymph nodes and liver were found to be present. This patient died a few days after surgery. Raiford also reviewed all of the car-

Presented at the Second Annual Meeting of the Central Surgical Association, Chicago, Ill., Feb. 27 and 28, 1942.

The physical examination revealed a well-developed, well-nourished woman with prematurely white hair, sallow complexion, and some evidence of weight loss. Pertinent physical findings referred to the abdomen. There was a well-healed right rectus shear from the xiphoid to a point just below the umbilicus and a healed McBurney's incision. There was slight tenderness to deep palpation along the right costal margin, but there were no masses palpable.

A diagnosis of recurrent peptic or marginal ulcer was made.

Urinalysis was negative. Blood count showed hemoglobin, 9.4 Gm.; 4,910,000 red blood cells; 6,250 white blood cells, with a normal differential count. Gastric aspiration showed 35° total acid and no free acid. Blood chemistry was within normal limits. Gastrointestinal x-rays revealed a normally functioning posterior gastroenterostomy with no evidence of a lesion in the stomach.



Fig 4.—Silver stain of tumor (high power, oil immersion).

On July 8, 1941, an exploratory celiotomy was done and a tumor about 6 cm. in diameter was found adherent to the stomach in the region of the cardia. A smaller tumor 1 cm. in diameter appeared within the gastric wall. Opposite the smaller tumor in the gastric mucosa was a healed ulcer. The gastroenterostomy was taken down and a gastric resection done. The patient's convalescence was complicated by the development of a bilateral bronchopneumonia and some difficulty in gastric emptying. She was discharged after twenty one days in the hospital on her nineteenth postoperative day, completely relieved of her symptoms.

Gross Description.—The specimen consisted of the stomach. Near the cardia was a small point of mucosal thickening with a central depression. Directly beneath the mucosa at this point was a tumor nodule 1 cm. in diameter. This was fairly firm and grayish yellow in color. Adjacent to this was a well encapsulated mass 7 × 6 × 5 cm. which on cut surface showed a grayish yellow color similar in appearance to the small nodule found in the stomach.

Microscopic examination showed numerous solid groups of cells, similar in appearance but poorly outlined and arranged in a fairly fibrous connective tissue stroma. The cytoplasm of these cells was vacuolated. The nuclei were large, equal in size, and had a good complement of chromatin. Mitotic figures could be found, but they were not numerous. One section showed a short strip of gastric

severe upper abdominal pain of ten days' duration. This occurred at about six month intervals until December, 1927, when she had a severe gastric hemorrhage. In March, 1929, a gastroenterostomy was done by her local surgeon. She had a rather difficult recovery period and was in the hospital twenty-two days. The patient felt quite well until December, 1929, at which time she had another hemorrhage; since then she has had episodes of hemorrhage two or three times a year.

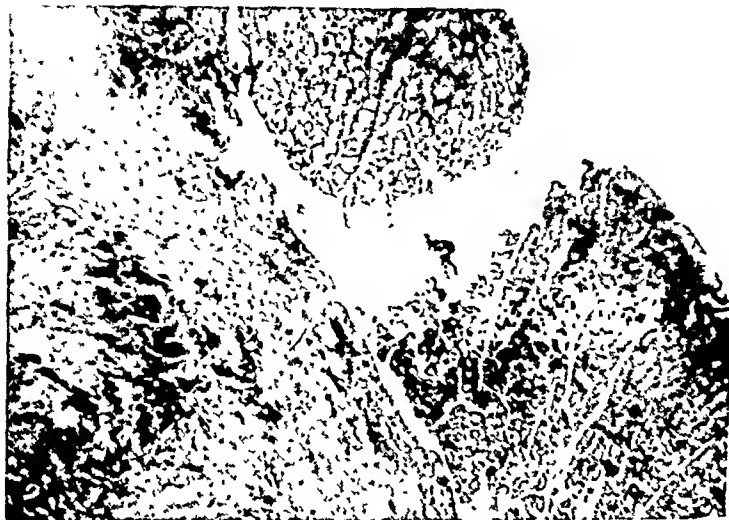


Fig. 2—Cross section of stomach and tumor (low power).

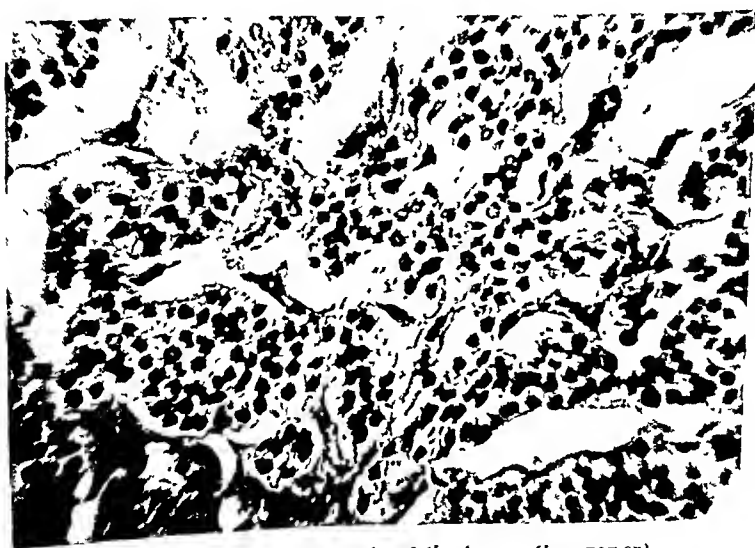


Fig. 3.—Hematoxylin and eosin of the tumor (low power).

On June 3, 1941, a severe hemorrhage occurred which necessitated four blood transfusions. Since then she has had pain high in the epigastrium which would frequently radiate to the right side of her back. The patient had an appendectomy in 1920 but no record of this operation was available.

REPORT ON 230 CASES OF SUBTOTAL GASTRIC RESECTION FOR PEPTIC ULCER

G. GAVIN MILLER, M.D., MONTREAL, CANADA

THIS group of cases has been operated upon by me mostly during the past five years, although I have advocated subtotal resection as a routine procedure for the past ten years, that is, since I was Professor Finister's assistant in 1930 and 1931.

These cases comprise all types of ulcers, simple, penetrating, perforated, pyloric stenosis, gastric, duodenal, stomal, and jejunal ulcers, and those complicated with gross and massive hemorrhage.

Seven deaths occurred, a mortality of 3 per cent.* The largest consecutive series with no mortality was ninety-three, demonstrating the fallacy of mortality figures in small series.

This series includes all the cases of peptic ulcer I have received, except seven in which palliative procedures were carried out. Two patients whose ulcers had been perforated for more than twelve hours before operation, received only simple closure of the ulcer. Two with pyloric stenosis were treated with gastroenterostomy, one at the request of the referring physician, the other because of cardiac decompensation. In two cases of massive hemorrhage, one was treated by ligation of the bleeding vessel and the other by ligation of the pancreaticoduodenal vessel and gastroenterostomy. The final case had a gastric ulcer extending from the esophagus to the pylorus and was considered an inoperable carcinoma until a biopsy specimen was reported to show only inflammatory tissue.

The average duration of symptoms in this series was eight years, the condition having persisted in spite of medical treatment. Except for the cases of perforated ulcer, all cases had been referred for operation by a physician, or a physician's recommendation for surgical intervention had been obtained.

The seven patients who died were autopsied with the following results.

1. Death occurred one month after operation from intestinal obstruction. This patient had a penetrating ulcer and was drained. He was an elderly, emaciated man, who developed wound infection, the wound broke down and required secondary sutures. The small bowels attached themselves to the scar, causing intestinal obstruction. Since then no patient has been drained unless drainage was especially indicated.

2. Death occurred from a necrotic perforation of the duodenum, one inch distal to the inverted stump. This was probably caused by the

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*Since this paper was written twenty further cases have been operated upon with no increase in mortality, giving a percentage mortality of 2.8 per cent.

mucosa which was sharply demarcated from the underlying tumor. Sections stained with silver show the characteristic deposition of silver salts within the cytoplasmic granules. A diagnosis of carcinoid tumor of the stomach was made.

The histogenesis and pathologic picture of carcinoid tumors has been fully discussed by Gosset and Masson, Raiford, Forbes, and others. It is generally agreed that this type of tumor arises from the chrome cells near the basement membrane of the crypts of Lieberkühn in the gastrointestinal tract. It is interesting to note that the gastric hemorrhage was undoubtedly due to the ulcer opposite the smaller nodule. This case is presented to call attention to the occurrence of a fairly common type of tumor in an uncommon location.

REFERENCES

1. Ewing, James: *Neoplastic Diseases*, Philadelphia, 1940, W. B. Saunders Company, pp. 723-725.
2. Gosset, A., and Masson, P.: *Presse méd.* 22: 237, 1914.
3. Humphrys, E. M.: *Am. J. Cancer* 22: 765, 1934.
4. Plaut, A.: *Arch. Path.* 28: 723, 1939.
5. Walley, G. I.: *St. Barth. Hosp. J.* 44: 141, 1937.
6. Raiford, T. S.: *Am. J. Cancer* 18: 803, 1933.
7. Pettinari, V.: *Arch. ital. di chir.* 40: 695, 1935.
8. Entwisle, R. M.: *Pennsylvania M. J.* 40: 1026, 1937.

One case was readmitted for investigation because of complaints of various residual symptoms. X-rays showed a normally functioning stoma, no free acid, hemoglobin of 90 per cent, and no occult blood in the stool. A psychiatric consultation made a diagnosis of anxiety neurosis.

Another patient put in the improved class in this series, who had four previous stomach operations, complains of colitis but is able to work and his family physician considers him cured.

Another patient complains of nausea and pallor. He insists on dieting and will not eat anything which he believes at any time has produced symptoms. His hemoglobin fell to 60 per cent but rapidly rose to 84 per cent when he was given iron and liver therapy.

The remainder of the seventeen we have classed as improved complain of vague symptoms, not similar to their ulcer symptoms, such as weakness, pallor, nausea, and loss of weight, but investigation by x-ray, gastric analysis, and in some of them by gastroscopic examination fail to disclose any new ulcer.

The majority of patients do not gain weight very easily but are adequately nourished. I know of no more grateful patients than this group who have been resected for ulcer.

It has been my experience, following this operation, that not infrequently a few residual complaints remain for a few months, such as hot flushes after drinking liquids, belching after meals, occasional nausea, and very occasional anemia. Some patients find it difficult to gain weight, although recently one came to me for a reducing diet. As time passes, however, these patients gradually lose the symptoms as the small stomach adapts itself to its new work.

A few further facts found in this series may be of interest. One hundred twenty-five cases were duodenal ulcers, fifty were gastric, seventeen pyloric, nineteen jejunal, and seven were doubtful from the operation note. Four patients had both gastric and duodenal ulcer. Three of the gastric cases showed malignant change. In one of these the changes were not noted in the sections but the patient developed bilateral Krukenburg's tumors six months later. In this case the base of a penetrating gastric ulcer was left in situ.

Eleven of these cases were resections for perforated ulcers, with one death from pulmonary embolus (9 per cent mortality). It is my feeling that in early perforations, that is under twelve hours, a resection is technically feasible, it will prevent further recurrence of the ulcer with the necessity of a second later operation, and will give a low mortality. The operation is, I must confess, more difficult than the usual case, owing to the thickened inflammatory wall of the duodenum. I am not yet prepared to advocate this procedure for routine use.

Our experience with early resection for gross and massive hemorrhage has been most encouraging. In the ten cases resected for massive hemorrhage, where immediate operation appeared indicated, we have had no

application of an Allis clamp at this point to facilitate the inturning of the duodenum. Since then a new clamp has been designed which will not damage the delicate wall of the duodenum, but even so, these clamps are not placed on the duodenum but on adjacent tissue to support the duodenum during closure.

3. Death was caused by leakage of the duodenal stump due to inadequate closure. The patient had a penetrating ulcer of the duodenum which would not be removed, therefore the duodenum was cut through at the pylorus. In such a case an exclusion operation is advisable.

4. Death was due to section of the common bile duct, causing bile peritonitis. In a large calloused penetrating duodenal ulcer of the duodenum the common duct was drawn into the mass and was cut and ligated without being seen. Careful exposure of the duct is essential in such cases.

5. Death was due to gangrene of the stump following an exclusion operation in a patient who had previously had a pyloroplasty and now had a penetrating ulcer with stenosis. In removing this mucosa the outer walls were damaged and left too thin, so that the blood supply was inadequate.

6 and 7. Death was due in both of these cases to pulmonary embolus. We are now doing eoagulograms on these patients and prolonging the bleeding time with coumarin.

There would appear little doubt that the next series should show a lowered mortality.

Of these 230 cases, attempts have been made to follow up the first 200, the last 30 being too recent to be of interest. Altogether, 173 cases have been followed, 110 by questionnaire and 63 by personal interview, that is, 85 per cent. Four patients have died since operation: one from tuberculosis, one from lymphosarcoma, one from Krukenberg's tumors and liver metastases, and the other from cerebral hemorrhage. Autopsy on two of these showed no recurrence of the ulcer, one and three years postoperatively. The other two had remained free from symptoms up to the time of their death, one and six years postoperatively.

Three patients have been operated upon since their gastrectomy and all three were found to have no new or recurrent ulceration. Two were opened for appendectomy and the opportunity was taken to explore the abdomen. The third, in whom the presence of ulcer was not definitely established at operation, was not improved by resection; one year later a careful exploratory operation showed no ulcer present in the stomach, duodenum, or jejunum.

Of the remaining cases followed, we can say that 90 per cent were cured and 10 per cent improved. In this series there has been no proved case of recurrence. Four cases are freed from their stomach symptoms but have cholelithiasis which gives some residual symptoms at times. Recheck of two of these shows a normally functioning stomach with no free acid.

oxon to each case, collect a urine specimen in five hours, and then quantitatively estimate the amount of C by the use of the dye sodium dichlorophenol-indophenol. If the patient is deficient in C, we administer the vitamin in sufficient quantity to change the reaction of the urine to the dye, both pre- and postoperatively.

Thus far we have studied 24 cases of peptic ulcer from this standpoint. In 18 cases of duodenal ulcer, 11 have been deficient and 7 sufficient. In 4 cases of gastric ulcer, 2 have been deficient and 2 sufficient. In 2 stomal ulcers, both have been sufficient. However, one case of combined gastric and duodenal ulcer, and one case of combined stomal and duodenal ulcer, have both been deficient. These figures tend to show the importance of testing for vitamin nutrition, inasmuch as 54 per cent of the cases have a definite C deficiency. We believe that we have less infection and better wound healing since the use of this test and the administration of vitamin C, for there has been no delay in healing and no infection in any of the cases which were closed without drainage (23 of 24).

It is interesting to follow up a series such as this. One is impressed by gratefulness of the patients, the freedom from visits to the doctor or hospital, their enjoyment of food, and I regret to say, too often of drink (alcoholic). Repeatedly patients have asked me why they could not have had this operation years earlier. That is a question I cannot answer for, of course, many of them should have had it years earlier. The average physician still fears the high mortality and the high rate of recurrence of bygone years. I hope that this report will overcome this fear, and that the next decade will see fewer painful sufferers condemned to Sippy diets and alkaline powders when cure can be offered them so easily. Our patients rarely spend more than two weeks in the hospital and are usually back at work after one month.

ADDENDUM

Since this paper was given two patients have been readmitted with gastrointestinal hemorrhage, one, seven years, and one, one year after operation. Neither had any gastrointestinal symptoms, x-ray showed no stomal ulcer, and both had free acid of 18 and 20 after an alcohol test meal. Gastroscopic examination revealed no ulcer. These cases may be considered as recurrences although they are not proved. Both have recovered and have had no symptoms since.

deaths. By massive hemorrhage, I refer to those cases with persistent bleeding, collapse, falling blood pressure, and low hemoglobin. The large single hemorrhage, accompanied by fainting with prompt recovery, I classify as gross hemorrhage; these offer no unusual risk. This series consists of eighty-three cases with a previous history of gross or massive hemorrhage and no operative deaths. Peculiarly enough, we have found the penetrating ulcer the most serious of all, all of our deaths falling into this group, except the two which resulted from pulmonary embolus.

Our rule in the cases of massive hemorrhage, if the patient is under 45 years of age, is to wait and see if the bleeding will not stop in the first forty-eight hours. Over 45 years, we advocate almost immediate surgical intervention, as in this group the mortality, under medical regimen, will approximate 35 per cent.

It has been mentioned already that no particular dietary regime has been ordered postoperatively. Resection appears to be the operation with the best chance of curing an ulcer. A few points in the post-operative care may be mentioned. After the operation there is a tendency for fluids to pass rapidly out of the stomach into the jejunum. Thus, if the liquids be hot, or perhaps even very cold, they tend to cause a hot flush and a feeling of faintness to come over the patient during the early postoperative months. They should be warned about this and advised to eat solid food at the beginning of the meal.

It has been found difficult in quite a few cases to obtain a gain in weight. The stomach for the first few months empties quickly and the food is not quite thoroughly digested and absorbed. Later the stomach holds the food longer. It is wise, therefore, for these patients to eat extra, small meals between their regular meals and upon retiring. This failure of absorption is probably the cause of the secondary anemia which is occasionally seen. For this reason our patients are advised to take iron and liver the first few months; this avoids any tendency to anemia. Since the vitamin intake should also be adequate, we give extra vitamins as a tonic. For the first six to nine months, some vague symptoms such as belching may be present, therefore, it is wise to forewarn the patients so they will not worry about the possible recurrence of their ulcer.

About three months ago, we became interested in the preoperative adequacy of the vitamins in ulcer cases, especially vitamin C, because of the relationship to susceptibility to infection and wound healing. In order to simplify the determinations, my resident has used the urine excretion test for vitamin C, since the amount of C excreted in the urine after the administration of a large dose is proportional to the C level in the body. As a state of body saturation approaches, the urinary excretion increases and the quantity of C necessary to effect saturation and adequate recovery in the urine is a simple test for the state of vitamin C nutrition of the patient. We use 150.0 mg. of red-

death from recurrence in three months, does not commend this method of treatment, it seemed advisable to report this case for two reasons. As yet, there are on record relatively few reports of cases in which the duodenum has been resected. A recent compilation published by Hunt³ shows a rapid progressive increase in the application of the operation and progress in its technical betterment. In all except our case, so far as we are able to ascertain, the operation has been performed for carcinoma involving the duodenum. It is probable that the indications for the operation will be expanded to include not only the very rare resectable sarcomatous and inflammatory lesions but possibly on a rare occasion some lesion such as a duodenal fistula associated with a much mutilated duodenum.

REFERENCES

1. Prey, D., Foster, J. M., and Dennis, W.: Primary Sarcoma of the Duodenum, *Arch. Surg.* 30: 675, 1935.
2. Whipple, H. O., Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, *Ann. Surg.* 102: 763, 1935.
3. Hunt, V. C.: Surgical Management of Carcinoma of the Ampulla of Vater and of the Periapillary Portion of the Duodenum, *Ann. Surg.* 114: 570, 1941.

PRIMARY SARCOMA OF DUODENUM; RESECTION WITH HEAD OF PANCREAS BY ONE-STAGE WHIPPLE OPERATION

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PRIMARY neoplasms of the small bowel are infrequent, malignant ones comparatively rare, and sarcomas of the duodenum very rare.

All proved primary sarcomas of the duodenum reported in the literature previous to 1935 were collected by Prey, Foster, and Dennis.¹ They were able to assemble only sixty-one authentic cases and reported one of their own. Their report revealed a large predominance of lymphosarcomas. There was essentially an equal numerical distribution of the other cell types, spindle cell or fibrosarcomas, myosarcomas, melanosarcomas, and myxosarcomas. Although these tumors frequently attain considerable size, they do not as a rule cause obstruction of either the duodenum or common bile duct. They usually cause much pain, anorexia, and a rapid loss of weight and strength. Necrosis within the tumor is common and not infrequently this results in hemorrhage or in perforation of the wall of the duodenum with fistula formation.

The occasional relatively benign myosarcoma can often be excised without sacrificing the duodenum. The other types of sarcomas are usually too diffusely disseminated for surgical extirpation. On a rare occasion, however, there may be sufficient circumscription of the tumor to warrant radical excision of the duodenum. This is also true of the still rarer inflammatory granulomas of the duodenum. What appeared to be an indication of this kind led to resection of the duodenum in the case which we are reporting.

This patient, a woman 42 years of age, was explored with the erroneous pre-operative diagnosis of cholecystoduodenal or choledochoduodenal fistula. This diagnosis was made from the radiographic visualization of the common bile duct filled with barium refluxed from the duodenum. Finding the wall of the first and second portions of the duodenum much thickened by what appeared to be either inflammatory or neoplastic infiltration, a biopsy was taken and examined immediately in frozen section. Because the pathologist made a provisional diagnosis from this examination, of chronic inflammation, and because the pathologic process appeared to be confined entirely to the duodenum, the first and second portions of the duodenum and the adjacent portion of the head of the pancreas were excised. The operation was performed in one stage; otherwise it was essentially the operation described by Whipple, Parsons, and Mullins,² in 1935.

Not until the permanent sections of the tissue had been studied was a final and correct diagnosis of lymphosarcoma made. Although the result in this case, freedom from symptoms for only two months and

quite impossible to locate accurately the pyloric ring. Most surgeons recommend that the affected portion of the duodenum together with the ulcer should be excised under these circumstances, but everyone, I am sure, who has carried out this procedure in a difficult case will admit that it is by no means easy. The fibrous tissue may be so dense and thick that the duodenal wall may be difficult to recognize and even when resection has been successfully accomplished, the amount of duodenum left may be insufficient to obtain a safe closure owing to the proximity of the bile duct. The object in performing a partial removal of the stomach for duodenal ulcer is the disappearance of the lesion and it would seem wise to accomplish this by the simplest and quickest method, provided the end results are satisfactory. It is not necessary to remove the ulcer, for if the gastric contents can be permanently prevented from coming in contact with the ulcer, it will heal.

In carrying out the procedure which we recommend, the pyloric antrum is freed in the usual fashion down to and including the pyloric ring, or if this is difficult to recognize because of the intensity of the scarring, as far as the head of the pancreas. A single clamp is then applied to the stomach about an inch and one-quarter from the pyloric ring and the stomach severed by the cautery close to the distal side of the clamp which, with the proximal portion of the stomach, is then laid aside. The free edge of the stump is then grasped by three forceps at suitable intervals leaving the mucous membrane free, however, and a sucker is introduced to cleanse the duodenum. The mucous membrane is then removed from the cuff as far down as the pyloric ring, after the method of Bancroft. It is very easily detached until the pylorus is reached and if the vessels on either side have been ligated right down to the ring it is likely that very little bleeding will be encountered. The next maneuver is to invaginate the musculoperitoneal cuff into the duodenum and suture it there. To this end it is necessary to determine the size of the opening into the duodenum and this may be estimated by means of the sucker apparatus or the insertion of an index finger. If the latter can be passed readily and the induration about the ulcer is moderate in amount, invagination is quite a simple matter. The duodenum is grasped just distal to the pylorus with three pairs of Allis forceps placed at equal distances, and while the duodenum is gently supported by careful traction on these forceps, the operator, after ascertaining the exact direction for the invagination, takes hold of one edge of the cuff with a plain forceps and pushes it in as far as it will go. Then while it is held there the central edge and finally the opposite corner are dealt with similarly. If successfully accomplished, the cuff will remain in position when the forceps have been removed and nothing remains to be done except to oversew with a double row of catgut suture and tie in some of the adjacent gastocolic ligament over the suture line. But if the opening into the duodenum is small and associated with con-

THE MANAGEMENT OF THE DUODENUM IN GASTRIC RESECTION FOR DUODENAL ULCER

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ALTHOUGH a variety of surgical procedures has been advocated, from time to time, for the relief of duodenal ulcer, it is now generally conceded that surgery should not be recommended except for very specific conditions. In order of their urgency these may be listed as acute perforation, massive gastric hemorrhage, duodenal stenosis, penetrating ulcer and one which fails to respond to efficient medical care. Acute perforation may be dismissed because resection of the stomach or a gastroenterostomy is never warranted under such a circumstance, as there is no necessity whatever to unduly narrow the lumen in effecting the closure. Massive hemorrhage, however, is in a different category inasmuch as there is a decided trend at the present time to do a resection in these cases, especially in an individual who has reached the age where arteriosclerosis makes spontaneous cessation of the bleeding less likely. Personally, I favor such a procedure provided one knows that a duodenal ulcer is actually present and operates as soon as it is apparent that the patient is slipping in spite of adequate medical care. Using the technique hereinafter described, we have done, in the past two and one-half years, a partial gastrectomy in nine consecutive cases for massive duodenal hemorrhage and all recovered without further bleeding. This is admittedly a very small series but still significant. Duodenal obstruction calls for some form of operative relief but there is considerable diversity of opinion as to whether a gastroenterostomy should be done or whether a partial gastrectomy is best. Unless the patient is well beyond middle life, my preference is for the latter procedure. This may carry a slightly higher operative risk but the convalescence is much more satisfactory and should be free from that very annoying, vicious circle vomiting which frequently follows a gastroenterostomy. And the end results are much more satisfactory.

While there are differences of opinion regarding the treatment of acute perforation, massive gastric hemorrhage, and duodenal stenosis, it is generally conceded that a partial gastrectomy offers the best chance for a permanent cure in cases of penetrating ulcer. In this type of lesion the common occurrence is an ulcer on the posterior wall of the first portion of the duodenum which has eroded into the pancreas. Varying degrees of inflammatory reaction are seen. In some there is little or no interference with the size of the lumen, while in others stenosis is a marked feature. Fixation of this portion of the duodenum is constant and there may be a firm mass a few inches in diameter in which it is

OBSTRUCTIONS OF THE SECOND AND THIRD PORTIONS OF THE DUODENUM

A REPORT OF FIVE CASES

M. M. ZINNINGER, M.D., CINCINNATI, OHIO

(From the Department of Surgery of the University of Cincinnati College of Medicine and the Cincinnati General Hospital)

WHILE obstruction of the second and third portions of the duodenum is a well-recognized clinical and pathologic entity, it is sufficiently rare to occasion some comment. An experience with five cases during the past five years has brought to my attention some of the problems and difficulties experienced in the diagnosis and treatment of lesions in this portion of the gastrointestinal tract which may be of interest to others. The varieties of obstruction which may be found at this level are well described in standard systems of surgery and in special texts and will not be reviewed here. The symptoms and signs are illustrated in the case reports which follow and will not be summarized. In most instances the clinician is dependent on the roentgenologist for the correct diagnosis, so to the latter must go the chief credit for recognizing obstruction at this level. It seems probable that many cases of partial obstruction are overlooked because of incomplete or inadequate roentgenologic study or improper interpretation.

CASE 1 —C F., a white male, 75 years of age, was admitted to the Holmes Hospital, Aug. 11, 1937, because of persistent vomiting. The onset was sudden, five days before, when he suddenly began to vomit without any pain or discomfort and with very little nausea. The patient attributed the trouble to having eaten too much at a banquet two nights previously. He continued to vomit small amounts frequently and could retain nothing by mouth. After five days he was sent to Cincinnati from his home in Kentucky. After decompressing his stomach by continuous gastric suction, a small amount of barium was given by mouth which apparently met a complete obstruction at the duodenojejunal junction (see Fig. 1). Several days later, after proper hydration, he was operated upon, and a curious condition was found. The jejunum was adherent by fairly recent adhesions along its antimesenteric border to the mesentery of the mid ileum. This mesentery was very long, and had undergone a torsion of approximately 180°. While this partial volvulus of the ileum had not produced strangulation or obstruction at this level, it had so twisted the jejunum at Treitz's ligament as to produce a complete occlusion at that point. This was readily relieved by untwisting the volvulus, freeing the adherent jejunal loop, and peritonealizing the raw surfaces. Recovery was rapid and uncomplicated.

Comment —The preoperative diagnosis of the etiology of the obstruction was obscure. Simple obstruction at this level is certainly uncommon. A right inguinal hernioplasty had been performed elsewhere six

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siderable induration this procedure must be modified by splitting the cuff. Since the penetrating ulcer is never on the anterior surface of the duodenum, the anterior portion of the cuff is selected for the incision, which runs parallel to the long axis of the cuff and should go far enough to divide both the pylorus and the constricting ring. When the split edges of the cuff are retracted it is converted into a triangle near the apex of which may be seen the musculature of the pylorus bulging into the lumen, and just beyond this, the penetrating ulcer. It will then be found that a finger can easily be passed into the duodenum. A purse-string suture is best in this case because the central portion can be pulled out in a loop and the duodenum steadied between this and the free ends. Before putting in the suture it is advisable to mobilize the second portion of the duodenum on its outer surface so that it will be free to be pulled readily toward the pancreas when the purse string is being tightened. The suture should commence on the outer surface of the duodenum about one-quarter of an inch away from and a little below the apex of the split. It should then pass around the duodenum to the spot corresponding to the point of entrance. When the posterior surface of the duodenum is reached, care must be taken not to go too close to the pancreas because of the danger of opening into the ulcer. The central portion of the purse string is then pulled out as a traction loop, and while an assistant steadies the duodenum with the suture, the upper angle of the cuff is grasped by a pair of smooth forceps and passed into the duodenum as far as it will go. If there is a strong tendency for it to come out, it should be held in place by a suture. The central and finally the lower angle are similarly dealt with and the purse string is tightened. A second suture is then inserted and a piece of adjacent gastrocolic ligament pulled over the suture line and held in place by tying the ends of the last suture over it.

COMMENT

A new method of dealing with pathologic conditions of the first portion of the duodenum is described, which we think lowers the mortality rate, saves a great deal of time, and is eminently safe. Although we have not had sufficient experience to speak dogmatically, we feel that it is the method of choice in resection for massive duodenal hemorrhage inasmuch as the muscular layer of the invaginated portion as it lies against the ulcer acts as an efficient muscle graft, and its blood-clotting properties may be further enhanced by pressure obtained by narrowing the lumen of the duodenum by suture.

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duodenum. Fluoroscopically, barium could be followed to the junction of the second and third portions of the duodenum. Reverse peristalsis then occurred and most of the material regurgitated into the stomach. A diagnosis of chronic duodenal obstruction was made, probably due to compression of the duodenum by the superior mesenteric vessels. After treatment for several months by diet, posture, abdominal massage, and antispasmodic drugs, without relief, she was operated upon. At operation (Fig. 2) the first and second portions of the duodenum were found to be dilated, the third portion contracted. Partial obstruction was due to the pull of the superior mesenteric vessels compressing the duodenum against the vertebral column. An antiperistaltic duodenojejunostomy was done easily. She ceased vomiting immediately and within six months had gained thirty pounds.



Fig. 2 (Case 2) —Findings at operation showing dilatation of second portion of duodenum and partial obstruction caused by pull of superior mesenteric vessels.

She has not remained entirely well, however. In January, 1939, an ovarian cyst was removed. Following this operation she began having occasional attacks of vomiting. In October, 1939, she was in the hospital for Raynaud's syndrome in both upper extremities. She also had a severe cystitis during this period. I did not see her again for several years, but she came under my observation again in the summer of 1941, complaining of epigastric pain and occasional vomiting. She weighed about 100 pounds at this time. X-ray showed a very atonic stomach low in the pelvis with the pylorus high. The barium left the stomach through the pylorus only when pushed up by the hand of the roentgenologist or when the patient was turned on the right side. There was no evidence of any ulcer, and the roentgen-

months before, but this could not be clearly related to the obstruction. No adhesions were found except those described above.

CASE 2.—T. D., a white female, 32 years of age, was admitted to the Cincinnati General Hospital in March, 1937, complaining of loss of weight and vomiting. At the age of 20 she had an attack of acute appendicitis, was operated upon, and was well for two years. At the age of 22 years, she was operated upon for hemorrhoids and rectal fissure and has had no rectal trouble since then. Immediately following this operation she began having epigastric pain after meals. This came on immediately after eating, lasted fifteen minutes to several hours, and was relieved by vomiting. For ten years she had vomited after every meal, and often after taking



Fig. 1 (Case 1) —X-ray showing marked dilatation of first and second portions of duodenum, and obstruction of third portion. The barium in the colon remains from a barium enema.

only water. She believed that she vomited only part of what was eaten, and therefore, ate again shortly after a vomiting attack. Eight years previously, at the age of 24 years, she was again operated upon and was told the uterus was removed because the bowel was adherent to it. At the age of 29 years, she developed gallstone colic with jaundice. Cholecystectomy was done at the Cincinnati General Hospital for cholecystitis with stones. According to the record, careful exploration at this time showed no obvious cause for the persistent vomiting. Removal of the gall bladder stopped the gallstone colic, but vomiting and epigastric pain persisted. At the time of appendectomy twelve years previously, she had weighed 135 pounds. Following the operation she gained until she weighed 180 pounds, two years later. When the persistent vomiting began she lost weight until at the time of this admission she weighed 85 pounds. The x-ray showed a marked saclike dilatation of the

time was 2900 c.c., the average amount 1000 c.c. X-ray on Feb. 13, 1939 (Fig. 3), showed the stomach to be dilated and atonic. The duodenal cap was deformed with a large ulcer niche in the central portion. The duodenum was markedly dilated in the first, second, and part of the third portion and presented active forward and reverse peristalsis and fibrillary movements. Abrupt narrowing of the caliber of the duodenum occurred at about the mid-point of the transverse portion. In the erect position no barium passed beyond this area. In the recumbent position, a thin stream of barium passed at intervals. At twenty-four hours no barium was found in the stomach. A diagnosis was made of duodenal ulcer and obstruction of the duodenum in the third portion probably due to pressure from without. Pain and gastric retention continued and on Feb. 25, 1939, operation was performed. A large duodenal ulcer with considerable scarring was found though the pylorus was patent. The stomach was very large. The first and second portions of the duodenum were very much dilated and there was marked obstruction of the transverse portion where the mesenteric vessels constricted it. About two-thirds of the stomach was resected, and a posterior Polya anastomosis done. On account of the marked obstruction in the third portion of the duodenum, a duodenojejunostomy was done to allow the bile and pancreatic juice free access to the jejunum. The patient had a smooth postoperative course. X-rays in March, and in September, 1939 (Fig. 4), show well-functioning stomas. He was last seen in the outpatient clinic in November, 1939, at which time he was very well and had gained fifteen pounds in weight. Verbal report in June, 1940, stated that he was free of gastric complaints.



Fig. 4 (Case 3).—X-ray taken in March, 1939, a few weeks after operation, showing function of both stomas.

Comment.—This patient showed tremendous gastric retention which was apparently due to obstruction in the third portion of the duodenum rather than at the pylorus, in spite of the fact that a large duodenal ulcer was present just beyond the pylorus. The method of origin and development of this obstruction is obscure. Vomiting during the last attack had been present for only a very short time. Relationship be-

ologist believed the epigastric pain was due to the pull of the low-lying stomach on the pylorus. The duodenum was normal in size, and when barium entered it progressed rapidly through into the jejunum by way of the stoma. By insisting upon her lying on her right side after meals, and lavaging her stomach once a day for several weeks to allow the dilated stomach to contract, the symptoms improved markedly. She gained twenty-five pounds in several months and then went on a reducing diet because she could not get into any of her clothes. When last seen early in January, 1942, she was feeling well, and there was no vomiting.

Comment.—This case evidently belongs to a group of chronic duodenal obstructions in which the mechanism of production is not clear. There is considerable difference of opinion as to how these patients should be treated. If any operative treatment is to be used, and it seems to be desirable to use it only in those cases of high-grade obstruction, the only rational procedure seems to be that used here. Many similar cases have been described in which the immediate result of the operation seemed to be satisfactory, but later the old symptoms all recurred. In this particular instance I believe that we have helped the patient considerably by the procedure used.



Fig. 3 (Case 3).—A, Anteroposterior x-ray showing dilated stomach with ulcer niche in duodenal cap. B, Lateral view showing dilated duodenum.

CASE 3.—O. C., a white male, aged 30 years, was admitted to the Cincinnati General Hospital Jan. 29, 1939, because of hematemesis and abdominal pain. The acute illness had started one week before with epigastric pain. Vomiting began two days before admission, and tarry stools and weakness one day before. The morning of admission there was a large hematemesis followed by loss of consciousness, and the patient was brought to the hospital in a state of shock. In the past history it was found that the patient had had symptoms of duodenal ulcer for thirteen years, beginning when he was seventeen years old with episodes of pain and vomiting about every six months, each lasting from one to three weeks. On admission the blood pressure was 88/60, lowest red blood count 3.46 million, and highest blood urea nitrogen 38 mg. per cent. The bleeding apparently ceased shortly after admission, but vomiting persisted. Frequent gastric expression was used, from 750 to 2500 c.c. being recovered. The largest amount obtained at one

probably due to extrinsic factors, most likely anomalous vessels, according to the roentgenologist. Active peristalsis was observed in the duodenum. Films taken at one, two, and four hours showed the same picture with no progress of the barium.

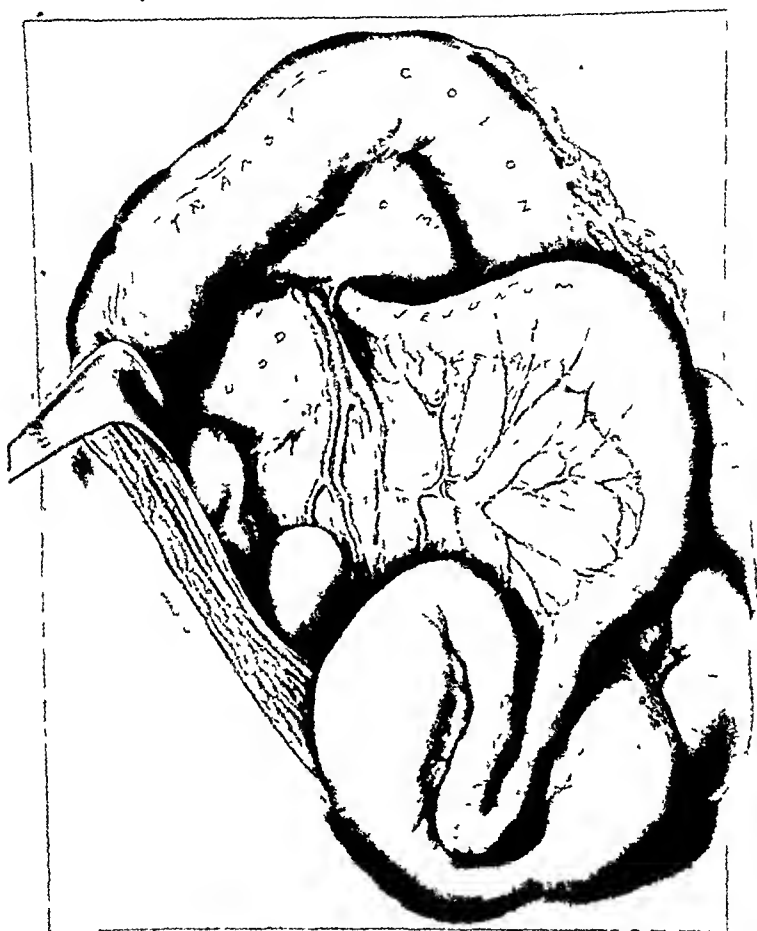


Fig 6 (Case 4) —Operative findings showing marked dilatation of the duodenum proximal to the superior mesenteric vessels, regional jejunitis, and constriction of the jejunum, with enlarged mesenteric glands

After hydration and repeated gastric expression the patient was operated upon, May 17, 1941. Marked dilatation of the duodenum was found up to the point where the mesenteric vessels crossed the transverse portion. In addition, a peculiar constriction of the first eighteen to twenty inches of the jejunum with marked thickening of the wall, was noted. The mesenteric glands to this segment of bowel were greatly enlarged (Fig 6). No other abnormality was discovered in the abdomen. The change in the bowel suggested a regional jejunitis, but on account of the extent of the lesion, especially the proximal extent beyond the ligament of Treitz, a resection was considered too hazardous for this patient in his depleted state. Accordingly an antiperistaltic duodenojejunostomy was done between the dilated part of the duodenum and the jejunum distal to the involved bowel. One enlarged

tween the ulcer and the obstruction does not seem to me to have been established. Some of you may think that the duodenojejunostomy was not necessary. However, the roentgenologic and operative findings indicated such a high-grade obstruction that it seemed advisable to me to perform it.



Fig. 5 (Case 4).—X-ray showing marked dilatation of duodenum.

CASE 4.—L. H., a white male, aged 26 years, employee of a coal company in West Virginia was admitted to the Holmes Hospital, May 12, 1941, complaining of weakness, loss of weight, and vomiting. He first noticed loss of appetite, and a feeling of fullness after meals beginning about nine to ten months previously. Partial relief was obtained by eructation of gas and vomiting of greenish, bitter fluid. The condition gradually grew worse until he vomited large quantities of fluid nearly every evening, about two hours after the evening meal. In February, 1941, a large gland, one of a chain in the right inguinal region was removed and a diagnosis of malignant lymphoma or early Hodgkin's disease was made. On arrival at Cincinnati he was emaciated, dehydrated, and the skin was deeply pigmented. There was moderate lymphadenopathy; the liver and spleen were not enlarged; the blood was normal except for a mild anemia. The night of admission 2 L. of fluid was drained from the stomach with a tube, and for the next few nights 800 to 1000 c.c. were aspirated at each gastric expression. X-ray May 14, 1941 (Fig. 5), showed the esophagus normal, and the stomach moderately dilated and filled with fluid. The barium could be easily expressed through a normal pylorus. The duodenal bulb, the second portion and part of the third portion of the duodenum were tremendously dilated. There was apparently no obstruction in the third portion,

grew worse with every dietary indiscretion or whenever he drank alcoholic beverages. More recent x-rays showed deformity of the duodenal cap suggestive of ulcer. The pain seemed to arise in the right costovertebral angle and radiate around to the right upper abdomen. He seemed to be making no improvement, and operation had been recommended by his physician. On Feb. 21, 1941, a laparotomy was done. The diverticulum of the stomach could not be located, though probably it lay in between peritoneal folds and surrounded by fat. There was no active duodenal ulcer present, though there was an insignificant scar, possibly of a healed ulcer. The head and body of the pancreas were noted as being firmer than normal. A pyloroplasty was done after incision of the duodenum was made to rule out an ulcer on the posterior wall. An appendix surrounded by adhesions was removed. Postoperative convalescence was smooth and he was discharged March 9, 1941, apparently well.

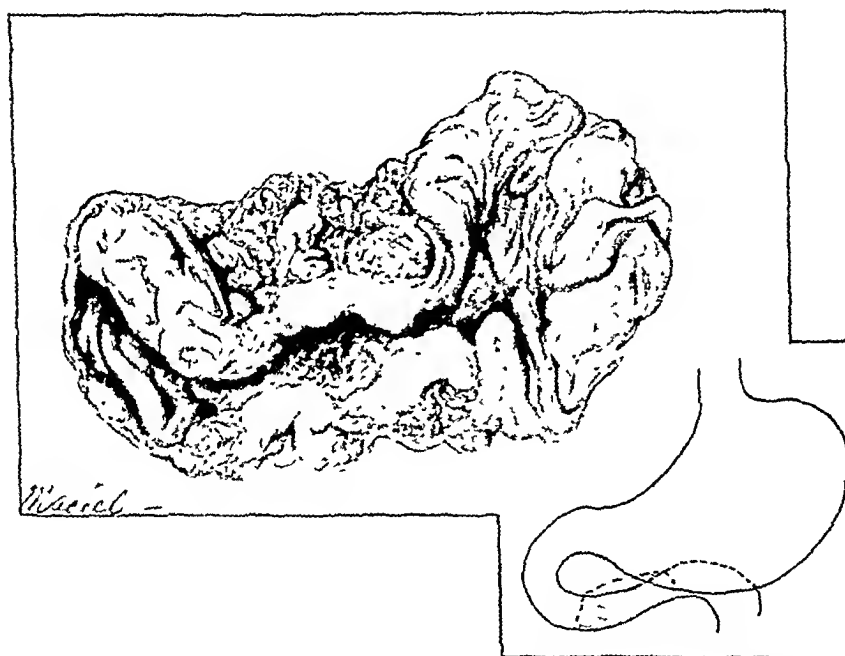


Fig 8 (Case 5).—Drawing of excised specimen, the ulcer in the center probably represents the cavity which resembled a diverticulum in the roentgenogram

He was readmitted March 25, 1941, because of recurrence of symptoms shortly after returning home. In addition to the pain, he now had occasional nausea and vomiting. Shortly after he entered the hospital an old urinary infection became reactivated and moderate fever developed. On March 31, 1941, barium was instilled into the small bowel by means of a duodenal tube. This showed normal position of all loops, normal motility, and normal outlines except in the third portion of the duodenum where there was noted a slight constriction and a constantly filled, irregular cavity about 1½ cm in diameter which was interpreted as a diverticulum (Fig 7). During this period the pain in the back became more intense, and vomiting increased, so that on April 12, 1941, operation was performed again. At this time a large, firm, annular mass was found constricting the third portion of the duodenum. This was resected with some difficulty due to its location between the

gland was removed and subsequent microscopic study showed only moderate hyperplasia both of lymphocytes and endothelial cells. The patient had a somewhat stormy postoperative course. He developed pulmonary atelectasis with high fever. Sulfathiazole was given in therapeutic doses, and he recovered without the development of a frank pneumonia. He left the hospital, June 4, 1941, the eighteenth postoperative day, apparently well. A report from his local physician in November, 1941, states that he is apparently quite well, eats what he likes, has gained weight and is working every day.

Comment.—Here again the reason for the development of the obstruction at the site where the mesenteric vessels cross the transverse portion of the duodenum is obscure. Could it be due to loss of weight and changes in intra-abdominal relations? Another factor was present here also, namely, the regional jejunitis. The question arises whether the sulfathiazole used in treating the pulmonary condition may not have exerted a beneficial influence on the lesion of the bowel.



Fig. 7 (Case 5).—X-ray of barium instilled into small bowel through duodenal tube, showing moderate dilatation of first and second portions of duodenum, the third portion shows a small barium-filled area with a constriction on each side. This central area remained constant throughout fluoroscopic examination and was regarded as a diverticulum.

CASE 5.—T. K., a white, male, 47 years of age, was admitted to the Holmes Hospital, Feb. 4, 1941. His principal complaints were nervousness, weakness, insomnia, and pain in the back and abdomen. Two years previously he had had an attack of hematemesis and tarry stools. A tentative diagnosis of duodenal ulcer was made. X-ray studies made some months later showed a small diverticulum of the stomach on the lesser curvature near the cardia. On a dietary regime he improved, but

THE USE OF SULFONAMIDES IN THE TREATMENT OF COMPOUND FRACTURES

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SINCE the introduction of the sulfonamides, hope has been entertained by many that by their use the incidence of infection in accidental wounds could be materially lessened. With few exceptions the oral administration of the sulfonamide group proved disappointing in the control of infection in compound fractures and its use was discontinued by most surgeons. The advantages of local implantation of powdered sulfanilamide in the wound was first brought to our attention by Jensen, Johnsrud, and Nelson, in 1939. They demonstrated, both clinically and experimentally, that the incidence of infection in contaminated wounds could be reduced materially by the introduction of sulfanilamide powder in the wound. They again emphasized the fact that the sulfonamides were a bacteriostatic and not a bactericidal agent and that in order to control infection in contaminated wounds it was necessary to have a higher concentration of the drug locally than could be obtained by oral administration. The local implantation of the drug in amounts of from 5 to 15 Gm. resulted in concentrations as high as 800 mg. per cent, which they felt was the factor in combating the infection locally.

Following this report a large number of articles appeared in the literature relative to the merits or demerits of this method of treatment in clinical cases. By far the majority of surgeons reporting on this were enthusiastic over the results obtained, although very few carried out or reported a control series. It is a difficult task to evaluate results accurately in the treatment of compound fractures unless we know all the facts pertaining thereto, such as the severity of the fracture, time seen after the accident, whether a dirty or clean wound, etc. Perhaps some of the discrepancies in the results obtained in different centers are due, in large part, to the difference in the local conditions. Prior to the use of sulfanilamide, the general infection rate with compound fractures at the Minnesota General Hospital ran from 25 to 28 per cent and this was reduced to 4.9 per cent following the use of sulfanilamide locally. At the Henry Ford Hospital the infection rate with compound fractures in 1938 was 20 per cent, and in 1939 it was 15.4 per cent. Since the use of sulfanilamide the rate has been reduced to 9.7 per cent.

A few of the reported results of treatment of compound fractures with local implantation of sulfanilamide are shown in Table I. Of those reporting, Campbell in particular questioned the efficacy of the drug but stated that further study and a larger number of cases would be necessary before a final conclusion could be reached.

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root of the mesentery and the aorta. It was necessary to take part of the body of the pancreas to which it was attached. An end-to-side anastomosis between the second portion of the duodenum and the jejunum was performed. Drains were placed owing to the incision into the pancreas. His postoperative course was relatively smooth considering the extent of the operative procedure. Gross and microscopic examination of the excised specimen showed an annular adenocarcinoma which almost completely occluded the lumen (Fig. 8). One of the preaortic lymph nodes removed with the tumor showed carcinomatous metastases. X-ray, May 20, 1941, showed a well-functioning stoma. The patient was discharged, apparently well, March 25, 1941, six weeks after operation. He remained well all summer. Repeat x-ray in November, 1941, showed the same findings as in March. According to the latest report in January, 1942, the patient is still apparently well.

Comment.—This patient was a problem from the beginning. He was extremely nervous, and it was impossible to evaluate his symptoms clearly. The roentgenologic evidence before the first operation was not absolutely conclusive, and operation was undertaken with some misgivings. No satisfactory explanation of his symptoms was found at this time, and evidently the lesion of the third portion of the duodenum was overlooked. On his second admission it was obvious that he had something fairly definitely wrong, organically. Again the evidence was not very conclusive. The presence of a lesion in the third portion of the duodenum was demonstrated roentgenologically only by passing a tube into the duodenum and instilling barium into the small bowel. However, the obstructive nature of the lesion was not fully demonstrated nor appreciated, and there was no indication of the serious nature of the condition. It seems unlikely that permanent cure can be expected since involvement of regional lymph nodes was demonstrated. The failure to recognize the presence of the lesion at the first exploration is certainly to be deplored. Careful review of the history and early x-rays fail to point to any evidence which would focus attention on this area.

The five cases here reported emphasize some of the difficulties experienced in the diagnosis and treatment of obstruction of the second and third portions of the duodenum. In general, the chief symptoms seem to be vomiting and loss of weight, usually without much pain. Duodeno-jejunosomy seems to be of definite value in the treatment of specially selected cases.

first few days, probably due to an excess amount of serous exudate, the wounds were completely healed in the same time as in the control animals. This observation was also found to be true with the amount of callus formation and time of fracture repair.

There is still a difference of opinion regarding the necessity of sterilizing the powder before placing it in the wound. Key has used autoclaved powder in his cases and reports no disturbance in the efficacy of the drug. We have not sterilized our powder because to date we have not felt that any harm resulted from the use of the fresh powder.

In the treatment of fresh compound fractures I would like to emphasize, as have so many others, the primary importance of sound surgical procedures. Under no circumstances does chemotherapy permit one to neglect a very thorough toilet of the wound. It has been our practice to carry out a débridement on fresh compound fractures that are seen in six hours or less following injury. The preparation of the wound and surrounding skin is carried out very thoroughly, using frequent changes of gloves, gowns, and drapes and copious irrigation of the wound with saline solution. We do not hesitate to use internal fixation whenever necessary, using wire, vitallium plates or screws as indicated. Sulfanilamide powder is placed in the wound in amounts of from 3 to 20 Gm., depending on the size of the wound. When possible to do so without tension, the wound is closed and a cast applied. Where there has been extensive loss of tissue the wound is left open, packed loosely with vaseline gauze, and a cast applied.

TABLE II
COMPOUND FRACTURES, PRIMARY CLOSURE

Number of cases	31
Time seen after injury	$\frac{1}{2}$ to 9 hrs.
	Average, 3 hrs.
Amount of sulfanilamide used locally	1 Gm. to 20 Gm.
	Average, 7 Gm.
Internal fixation (8 vitallium plates, 4 wire)	12 cases or 40%
Skin necrosis	13 cases
Infection (mild)	3 cases or 9.7%

TABLE III
COMPOUND FRACTURES, PACKED OPEN

Number of cases	10
Time seen after injury	1 to 7 hrs.
	Average, 4.2 hrs.
Amount of sulfanilamide used locally	1 Gm. to 20 Gm.
	Average, 9.5 Gm.
Internal fixation (wire)	2 cases
Infection	1 case or 10%

A total of forty-one fresh compound fractures have been treated in this manner. The results are shown in Tables II and III. Thirty-one of the cases were closed primarily and three, or 9.7 per cent, had mild

TABLE I
FRESH COMPOUND FRACTURES

AUTHOR	CASES	INFECTED	PER CENT INFECTED
Jensen	41	2	4.9
Speed	35	4	11.4
Swart	15	2	13.3
Breck	7	1	14.2
Stuck	21	2	9.5
Campbell	35	10	28.5
Total	154	21	13.6

Following the early reports of the use of the drug in the treatment of compound fractures, other writers cautioned against overenthusiasm and felt that overconfidence in its efficacy might lead to neglect of the all important surgical principles necessary to the toilet of a wound. Others felt that the older proved methods of procedure such as the Bipp, Orr, and Trueta methods should be continued until it could be shown that the results from the use of sulfanilamide were better.

The present war has provided a tremendous stimulus to the investigation of treatment of compound fractures and, as with all other wars, undoubtedly many lessons will be learned and great advances made in the treatment of this surgical condition. Primary closure of compound fractures in war surgery has always been condemned because of the high percentage of infections and amputations incident thereto. Trueta's closed plaster method used in the Spanish and present World War has proved very satisfactory and has been indorsed by almost all surgical observers. Many are now using sulfanilamide locally in addition to the vaseline pack and report a still lower incidence of infection. Very encouraging reports have been released from the Surgeon-General's office on the results of treatment of compound wounds with sulfanilamide in the recent disaster at Pearl Harbor. Large amounts of sulfanilamide were placed in the wounds either at the scene of the accident or immediately upon admission to the hospital. Reports state that these wounds remained clean and that it was possible to carry out a débridement as late as thirty-six hours after the injury.

Perhaps by the first-aid administration of the drug locally we will find that the infection rate is still further decreased. Certainly this type of treatment is worthy of further clinical and experimental investigation. Caldwell has recently demonstrated experimentally that sulfathiazole powder introduced immediately into a wound contaminated with *Bacillus welchii* will prevent gas bacillus infection in 100 per cent of the cases. When the powder was placed in the wound one hour after the introduction of the organisms, 77 per cent of the animals died of gas bacillus infection.

The objection has been raised that the sulfonamides locally implanted might delay wound healing and fracture repair. Key and others in experimental work have shown that although there is a delay in the

ACUTE COSTAL CHONDRITIS ASSOCIATED WITH STERNAL OSTEOMYELITIS

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ALTHOUGH acute infection of the costal cartilages and of the sternum occurs infrequently, the disease is, nevertheless, so serious as to justify the attention of every surgeon.

There are twelve costal cartilages on each side of the thoracic cage. The first five pairs are each articulated with the sternum. The next five are each articulated with the lower border of the cartilage of the preceding rib and the last two have pointed extremities.

There are three portions of the sternum, namely, the manubrium, the body, and the xiphoid process. Of interest is the xiphoid process, which in youth is cartilaginous, but becomes ossified in its upper half in adult life, the lower half still remaining cartilaginous.

Incidence of either acute costal chondritis or sternal osteomyelitis or both is probably less than one-half of 1 per cent of all cases of osteomyelitis.

The mode of infection is limited to two routes, namely, (1) hematogenous borne, and (2) accidental exposure of costal cartilages followed by immediate or delayed infection.

In making upper abdominal or lower thoracic incisions surgeons should be very careful not to expose the sternum or the costal cartilages in the presence of infection.

The most common and frequent early symptom is pain at the site of the infection. This may become excruciating pain during respiratory motion as the disease progresses. The local signs of inflammation are present. If there is abscess formation in the soft tissue of the chest wall fluctuant areas can be palpated. Not infrequently draining sinuses develop in a neglected case and they usually vary in number. The mortality rate of this disease is between 27 and 50 per cent.

As soon as the diagnosis is made of acute costal chondritis or of sternal osteomyelitis, alone, or associated, the treatment consists of adequate drainage of the infected area with resection of all involved cartilage or bone, or both, keeping in mind the fundamental surgical principles regarding infection in these structures.

If the chondritis is localized to any one of the first five costal cartilages the surgical principle of complete resection of that cartilage from the sternum and including the costochondral junction can easily be accomplished. However, when the second five pairs of costal cartilages are involved, namely, six, seven, eight, nine, and ten, the problem

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infection. A number of these cases developed small skin sloughs along the suture line but on most of these no infection followed. Of the ten cases left open, one or 10 per cent developed infection which was severe enough to necessitate amputation. No cases of tetanus or gas bacillus infection were encountered in this series.

SUMMARY

We believe, from an analysis of this small series, that sulfanilamide powder used locally in the treatment of compound fractures is an important adjunct to débridement in the prevention of infection.

It is suggested that the earlier or first aid administration of the sulfonamide drugs locally may still further reduce the incidence of infection. Further investigation of the method of treatment seems definitely worthy of consideration.

REFERENCES

1. Jensen, N. K., Johnsrud, L. W., and Nelson, M. C.: Local Implantation of Sulfanilamide in Compound Fractures; Preliminary Report, *SURGERY* 6: 1-12, 1939.
2. Campbell, Willis Cohoon, and Smith, H.: Fresh Compound Fractures; Treatment by Sulfonamides and by Internal Fixation in Selected Cases, *J. A. M. A.* 117: 672-675, 1941.
- Campbell, Willis Cohoon, and Smith, H.: Sulfa Drugs and Internal Fixation in Treatment of Compound Fractures, *South. Surgeon* 10: 409-426, 1941.
- Campbell, W. C., and Smith, H.: Sulfanilamide and Internal Fixation in Treatment of Compound Fractures, *J. Bone & Joint Surg.* 22: 959-972, 1940.
3. Trueta, J.: Treatment of War Wounds and Fractures, New York, 1940, Paul B. Hoeber, Inc.
4. Caldwell, G. A.: Treatment of Gas Gangrene Experimentally Produced, *J. Bone & Joint Surg.* 23: 81-85, 1941.
5. Key, J. A., and Frankel, C. J.: Local Use of Sulfanilamide, Sulfapyridine and Sulfamethylthiazol, *Ann. Surg.* 113: 284-297, 1941.
6. Key, J. A.: Use of Sulfanilamide and Sulfathiazole in Orthopedic Surgery, *J. A. M. A.* 117: 409-412, 1941.
7. Stuck, W. G., Maxwell, E. A., and Monsalvo, R. N. O.: Crystalline Sulfanilamide in Compound Fractures, *Texas State J. Med.* 36: 225-228, 1940.
8. Breck, L. W., and Basom, W. C.: Sulfanilamide Sulfathiazole Mixture in Compound Fractures, *M. Rec.* 154: 311, 1941.
9. Swart, Howard A.: Discussion on Key and Burford Article, *South. M. J.* 33: 449-455, 1940.

is somewhat more difficult. Again complete extirpation of the cartilage is essential and, therefore, it is not only necessary to resect the affected area, but also the entire mass of cartilage which joins these ribs to each other and to the sternum. This makes the operation one of magnitude, but it is the only procedure which is sure to be followed by success.

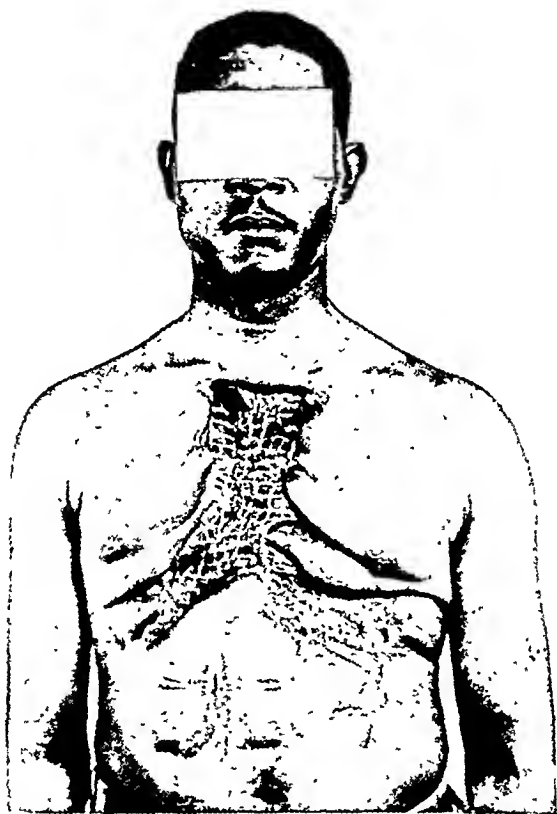


FIG. 4—View of anterior chest wall showing wound entirely healed and gastric fistula closed (December, 1941).

CASE REPORT

G. A., a colored male, aged 42 years, was admitted to the Cincinnati General Hospital, June 23, 1940, sixteen and one-half hours after an onset of severe epigastric pain. The diagnosis of a perforated peptic ulcer was made and through a short, upper right rectus incision a perforated duodenal ulcer was closed. At this time peritoneal fluid culture revealed three organisms, namely, *Bacillus aerogenes*, nonhemolytic streptococcus, *Staphylococcus aureus*.

The patient ran a septic course and on July 4, 1940, a left subhepatic abscess was drained through a left paracostal incision. There is some question as to whether the left costal margin was exposed or not at this time. An accidental gastrostomy was made and closed immediately. Soon after, the patient revealed signs of left costal chondritis. A gastric fistula developed.

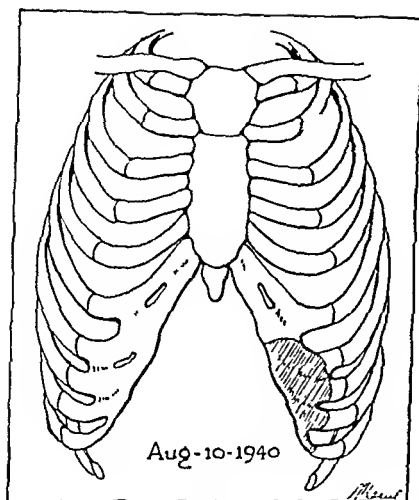


Fig. 1.

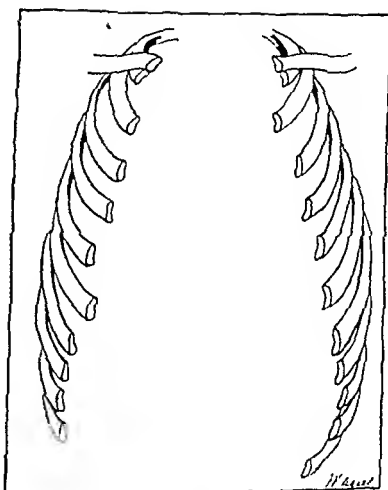


Fig. 2.

Fig. 1.—Diagrammatic sketch showing the original site of acute infection

Fig. 2.—Diagrammatic sketch of anterior thoracic cage after final resection



Fig. 3.—Anterior chest wall showing a partially grafted wound; catheter is in gastric fistula.

POSTOPERATIVE THROMBOPHLEBITIS AND EMBOLISM

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WITHIN the past few years it has been shown by a number of investigators that postoperative venous thrombosis, thrombophlebitis, and pulmonary embolism can be prevented definitely by the adequate administration of heparin. Recent studies of another preparation, dicoumarin, 3, 3'-methylene-bis-(4-hydroxycoumarin), indicate that adequate and closely supervised administration of this drug also will prevent these postoperative complications. However, heparin is expensive and somewhat difficult to administer and the dosage should be individualized for each patient, depending upon its exact effect on the coagulation time of the blood. This necessitates frequent determinations of the coagulation time. Dicoumarin is not expensive and is easily administered by mouth. The dosage of this drug, however, also must be carefully individualized, depending upon the results of daily accurate determinations of the prothrombin time. There is some risk of hemorrhage, during the administration of both heparin and dicoumarin, although this danger may be minimized by careful individualization of dosage. The tendency toward hemorrhage of heparinized patients can be stopped easily and quickly by discontinuance of administration of heparin and by the use of protamine. The effect of dicoumarin can be stopped by the transfusion of fresh, citrated blood, although sometimes not as rapidly as in the case of heparin, and it may be necessary to transfuse blood several times.

In a review of the records of 1,665 consecutive cases of postoperative venous thrombosis, thrombophlebitis, and pulmonary embolism, the incidence of all these complications was found to be only 0.96 per cent for all operations, 2.1 per cent for all cases of laparotomy, and 3.1 per cent for all cases of laparotomy in which surgical procedures were done on the female pelvic organs. The incidence of fatal pulmonary embolism was 0.2, 0.4 and 0.5 per cent, respectively, for these three groups of surgical patients. Thus, while postoperative thrombosis and embolism are serious complications, they are actually comparatively rare, and the use of either heparin or dicoumarin does not seem justified as a routine procedure to prevent thrombosis and embolism. To date, we know of no satisfactory test for determining which patients have a definite tendency toward postoperative thrombosis and embolism.

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On Aug. 10, 1940, when an attempt was made to close the gastrostomy, the involved cartilages (shown by the shaded area in Fig. 1) of ribs seven, eight, nine, and ten were partially resected. The infection continued to spread and the patient ran a septic course. The gastric fistula persisted and multiple draining sinuses of the left costal margin were present. Repeated culture revealed the organisms to be nonhemolytic streptococcus and *Staph. aureus*.

On Oct. 5, 1940, the block cartilages of six, seven, eight, nine, and ten remaining on the left side were resected. We were rather sure we had resected all of the involved cartilage. The wound was treated with daily wet dressings, but drainage was always seen in the region of the xiphoid process. *We now assume that the infection spread from the left to the right costal region through the cartilaginous tissue of the xiphoid process.*

On Nov. 3, 1940, it was necessary to resect the block cartilage of ribs six, seven, eight, nine, and ten on the right side as well as the xiphoid process and a small portion of the body of the sternum.

In spite of this radical procedure the infection spread to the cartilages of the fourth and fifth ribs and these were resected as well as over one-half of the body of the sternum, on Nov. 15, 1940. We were sure that after this procedure there should be no extension of the infection.

By Nov. 30, 1940, the cartilages of ribs two and three, the remaining body of the sternum, and part of the manubrium were involved and resected.

The infection continued an upward spread and on Dec. 14, 1940, the final resection was done. At this time the cartilages of the first ribs, the sterno-clavicular joints, and the remaining portion of the manubrium were resected (Fig. 2).

About twelve days after the final stage of resection this patient developed bilateral basal bronchopneumonia associated with labored respirations due to mechanical embarrassment of the thoracic cage. The patient was placed in a Drinker-Collins respirator, which we believe carried him sufficient time to allow the granulation tissue to overcome the mechanical difficulty. The wound was grafted in multiple stages (Fig. 3). This patient made a complete recovery and is now leading a normal life (Fig. 4).

In summary, we emphasize that acute costal chondritis associated with sternal osteomyelitis is a rare but serious syndrome. The importance of anatomic knowledge of the costal cartilages and the sternum has been stressed. Curability can result only through the application of surgical principles to the anatomicopathologic problem presented.

To our knowledge this is the only case where twenty costal cartilages and the entire sternum have been resected.

ASPIRATION BRONCHOPNEUMONIA

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PREVIOUS publications^{1, 2} have called attention to the frequency of occurrence and clinical manifestations of acute bronchopneumonia that results from the aspiration of regurgitated gastric material. It is the purpose here to point out the anatomic changes that must be present in order to demonstrate this form of pneumonitis in contrast to bronchopneumonia caused by the usual upper respiratory organisms such as pneumococci, *Micrococcus catarrhalis*, *Streptococcus hemolyticus* and *Str. viridans* in which the inflammatory process goes through the stages of engorgement, red hepatization, and gray hepatization very much like the stages of lobar pneumonia. The inflammatory reactions following the aspiration of gastric material are chiefly hemorrhagic, edematous, and hyperemic. Polymorphonuclear and fibrin exudation occurs infrequently. This condition in the past has frequently been interpreted both clinically and pathologically as hypostatic bronchopneumonia and hypostatic hyperemia and edema.

There are two general groups of predisposing causes. Whenever the gastrointestinal tract is dilated from paralytic ileus, bowel obstruction, or dilatation of the stomach, the chance for regurgitation is present. In other cases stupor and coma predispose to the aspiration of material from the pharynx and regurgitated material from the stomach because of loss of control of the laryngeal muscles.

It is desirable to perform the post-mortem examination within one or two hours after death in order to minimize the degree of post-mortem changes in the lung tissue. Lungs, ordinarily, do not undergo post-mortem changes rapidly. In the presence, however, of regurgitated material from the gastrointestinal tract such changes are observed soon after death.

When the sternum is removed the lungs do not collapse because they are distended with air. This is due to flooding of the bronchial tree with material from the stomach or hemorrhagic exudate interfering with expiration, as do all conditions that partially occlude the lumen of the bronchial tree.

Disseminated in the lungs, there are hemorrhagic, edematous, and hyperemic regions, increasing in extent from the anterior to the posterior portions. These regions, instead of having the red color of hemoglobin, very frequently have abnormal shades of color due to methemoglobin and hemolysis.

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In the statistical analysis of the 1,665 cases, it was found that approximately 50 per cent of patients having fatal pulmonary embolism had had previous episodes of nonfatal embolism or pulmonary infarction or had had clinically diagnosed thrombophlebitis. Of 381 patients who had pulmonary embolism or infarction and survived, 44 per cent were afflicted by a subsequent episode of embolism or thrombophlebitis, 30 per cent were afflicted by a subsequent episode of embolism, and 19 per cent subsequently had a fatal pulmonary embolism. Of those patients who had thrombophlebitis which was diagnosed clinically, 11 per cent had a subsequent episode of thrombophlebitis, 16 per cent had pulmonary embolism, fatal or nonfatal, and 6 per cent had a subsequent episode of fatal pulmonary embolism. The statistical study showed further that postoperative thrombosis and pulmonary embolism were two and one-half times as common among patients having carcinoma, three times as common among patients having diseases of the peripheral veins or severe infections, three and one-half times as common among patients having heart disease, and four and one-half times as common among patients having anemia or other evidence of blood dyscrasias, as it was in the group of patients who had none of these predisposing factors. It was found that the incidence of postoperative venous thrombosis or pulmonary embolism was very high among patients who had had thrombophlebitis recently (within six months) or pulmonary embolism occurring spontaneously or after another operation. There was a slight but definite increased incidence in these two conditions among those patients who had had thrombosis or embolism longer than six months previously.

At present we feel that the use of anticoagulant therapy, with either heparin or dicoumarin, is indicated for all patients who have had pulmonary embolism or pulmonary infarction and have survived. It is also indicated for patients in whom thrombophlebitis develops, because in these two groups the risk of further episodes of venous thrombosis and/or embolism and even fatal pulmonary embolism is sufficiently great to warrant great concern. We also found that heparin and dicoumarin should be administered postoperatively as a preventive measure to those patients who have had thrombophlebitis recently or pulmonary embolism arising from any cause within six months prior to the operation. Patients who have organic heart disease, varicose veins, anemia or other blood dyscrasias, carcinoma, or severe infections have a somewhat greater tendency toward postoperative venous thrombosis and pulmonary embolism than do patients who do not have these conditions. Although the use of heparin and dicoumarin is not advisable as a routine procedure, even in these groups, if a combination of several factors is present such anticoagulant therapy is usually indicated.

CONCUSSION OF THE LUNG

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HIGH-EXPLOSIVE bombs have been used more widely on the civilian populations and at sea in this World War II than in any previous conflict. For two years this country has been aware of the bombing of cities; consequently, a real need has arisen for the investigation of the nature of this urgent problem. One of the more significant problems of the present war thus becomes an analysis of the detonation of high explosive and its effect on the human body.

Injury resulting from high explosive was observed during the last war. At that time it was variously regarded as "shell shock" and "commotio thoracis." It was observed in soldiers who were near an exploding shell, but who were not actually hit by the flying fragments. Similar observations were reported from the Spanish Civil War and similar injuries have long been reported in civilian accidents in which the individuals were badly shaken up but at the time seemed to have escaped more serious injury. More recently, it has been frequently observed during the bombing of England. The British have carefully studied the condition, and have applied to it the general term of "blast injury" (Fig. 1).

Concussion of the lung, thus, on the basis of experimental studies of Zuckerman,² appears to be due to the effects of the blast wave which follows the explosion of a rapidly detonating projectile, such as a bomb. The explosion results in the sudden compression of the air immediately surrounding the bomb. Thus, at any point in the immediate neighborhood of an explosion, there occurs first a momentary wave of high pressure followed by a lesser one of negative suction pressure. The pressure recordings obviously vary with the distance and the size and weight of the bomb. For example, at a distance of fifteen feet from an exploding 125-pound bomb, the hydrostatic pressure may be as high at 200 pounds per square inch, whereas at a distance of fifty feet, the maximum pressure recorded will not be more than ten pounds per square inch (Fig. 2).

The pulmonary injuries were found to be directly due to the impact of the pressure wave on the chest wall, since the lesions were found to be localized to the side facing the explosion. When half the animal was protected with sponge rubber, no lesions were observed if the protected side faced the explosion, but characteristic lesions were observed

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The lining of the bronchial tree is usually the seat of an intense active hyperemia and superficial desquamation of the epithelial cells. The degree of hyperemia is more marked than is observed in instances of pneumococcal pneumonia. Furthermore, the mucosa is usually intact in the bronchial tree in ordinary bronchopneumonia, provided that tissues are fixed soon after death.

If the patient dies soon after aspiration, the material in the bronchial tree has many of the characteristics of the material found in the stomach. If a few hours have elapsed, the lumen is occupied by a hemorrhagic exudate.

Cultures are made of the blood in the right heart chambers, the material in the trachea, hemorrhagic lung tissue, and the lumen of the stomach. It is found that the bacterial flora in the trachea, lung, and stomach is the same and consists of organisms commonly found in the intestinal tract but not in the mouth or pharynx, such as gram-positive anaerobic bacilli, colon bacilli, yeasts, and occasional staphylococci. In most instances the cultures of blood from the heart are negative, indicating that the bacteria found in the lung tissue did not obtain their way through the blood stream from the gastrointestinal tract.

Histologically, the most common changes consist of extreme engorgement of the alveolar capillaries, disseminated regions of edema and hemorrhage, and decreased staining capacity of the lung tissue, in contrast to the distinctiveness observed in other organs. Occasionally bile pigment and undigested particles of food are observed in the bronchioles and alveolar spaces. It has been noted that polymorphonuclear leucocytes begin in the exudate several hours after aspiration.

Bizarre instances of advanced post-mortem change simulating acute gangrene of the lung have been observed in the past, beginning with the time of Becker's publication, in 1887.³ The edematous and hemorrhagic phase, which is the common one, has not been recognized etiologically by pathologists and physicians. Attention is called to the fact that aspiration pneumonia of this type occurs in individuals who have lost free hydrochloric acid in the stomach content which allows the development of a heavy bacterial flora in the gastric juice.

REFERENCES

1. Apfelbach, C. W., and Christianson, O. O.: Alterations in the Respiratory Tract From Aspirated Vomitus, *J. A. M. A.* 108: 503, 1931.
2. Irons, Ernest E., and Apfelbach, Carl Wesley: Aspiration Bronchopneumonia, *J. A. M. A.* 115: 584-587, 1940.
3. Becker, Ernst: Beiträge zur Geschichte der Aspirations pneumoniae (Göttingen), Helmstedt, 1887, J. C. Schmidt.

when the unprotected side faced the explosion. Bilateral lesions were not observed, thus, it appears that the etiology is a local rather than a general traumatic effect mediated through an open trachea. Injuries to the central nervous system are likewise thought to be caused by the hydraulic-like pressure developed from sudden compression of the thoracic cage with consequent violent back pressure on the venous side. The most frequent pathologic findings in blast injuries are ruptured alveoli, ruptured alveolar vessels, and evidence of traumatic pulmonary hemorrhage. A more recent report indicates that the lesions were also found in other organs, including the epicardium of the heart, and very frequently in the large intestine, which, next to the lungs, proved to be the most susceptible to the effects of blast. As a rule, there are no fractures and no external signs of injury.

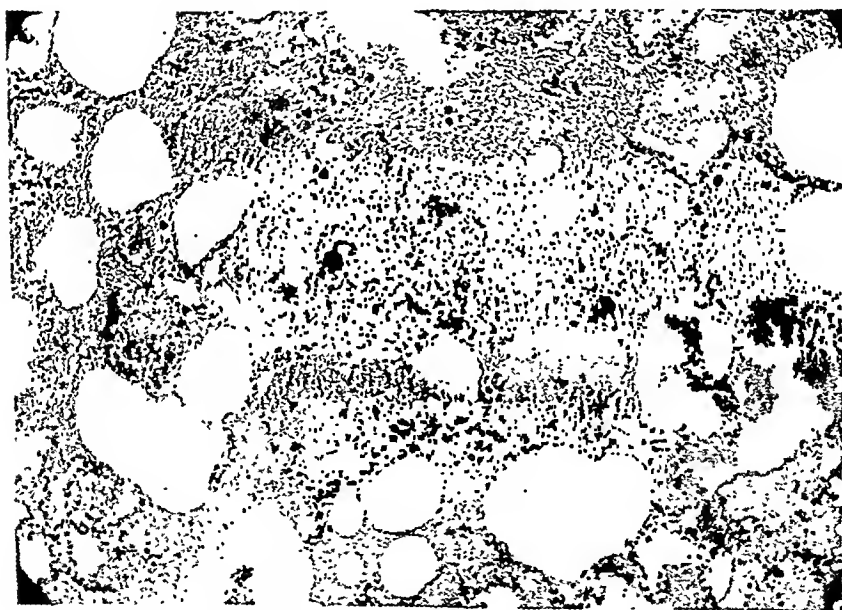


Fig. 3.—Photomicrograph of the lung after injury by contusion in peacetime civilian life. Note the hemorrhagic exudate in the ruptured alveolar spaces.

With evidence supporting the theory that the lung damage is due to the physical impact of the blast wave against the thoracic wall, attention is consequently directed to reported observations of such similar forms of lung injury in peacetime civilian life. It has been observed that such forms of lung injury occur more commonly in children than in adults. This is probably because of the more elastic nature of the thoracic cage in children in whom the lungs are more easily compressed between the resilient ribs. An example of this form of lung injury was observed recently in one of our own patients. A boy, 12 years of age, died soon after having sustained a heavy crushing blow on the

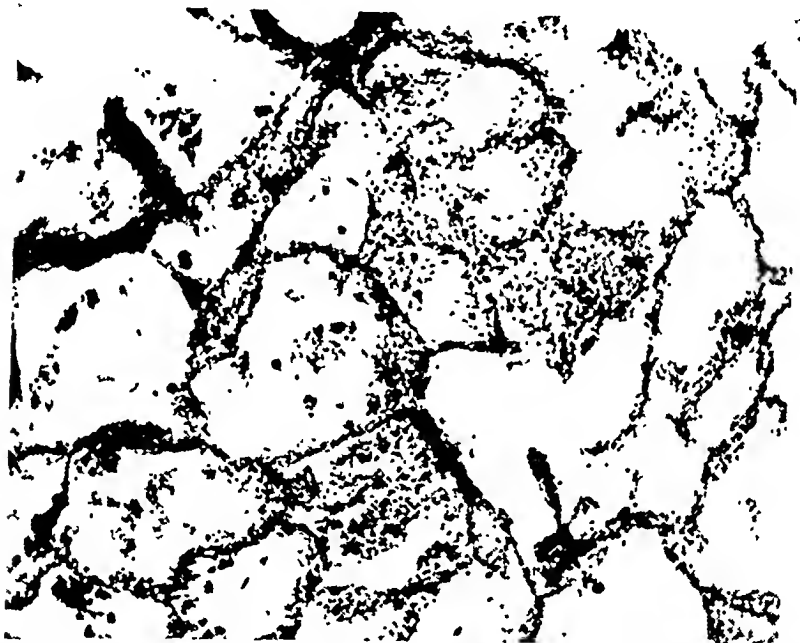


Fig. 1.—Photomicrograph of the lung of a man who died as a result of injury sustained in an air raid. The alveoli, which are disrupted, are filled with blood cells. (After Zuckerman.²)

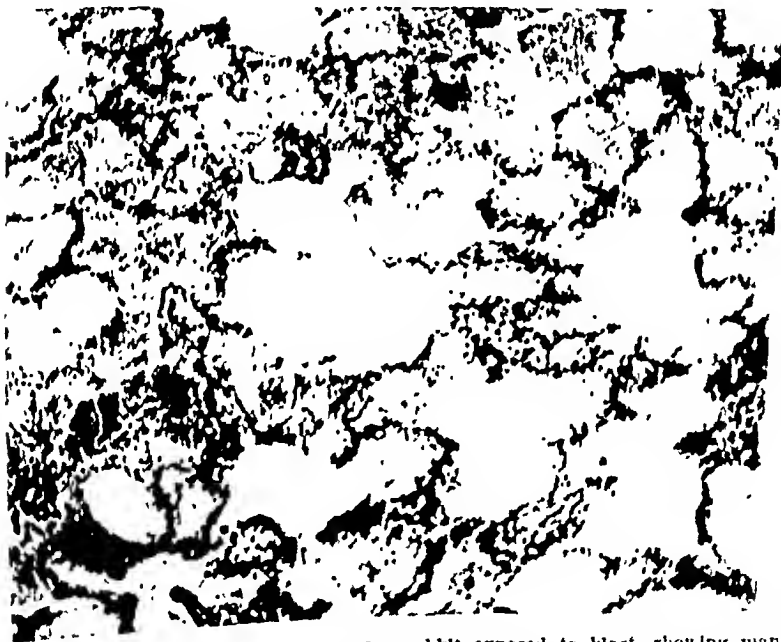


Fig. 2.—Photomicrograph of the lungs of a rabbit exposed to blast, showing many alveoli filled with blood cells, and the disrupted alveolar walls. (After Zuckerman.²)

when the unprotected side faced the explosion. Bilateral lesions were not observed, thus, it appears that the etiology is a local rather than a general traumatic effect mediated through an open trachea. Injuries to the central nervous system are likewise thought to be caused by the hydraulic-like pressure developed from sudden compression of the thoracic cage with consequent violent back pressure on the venous side. The most frequent pathologic findings in blast injuries are ruptured alveoli, ruptured alveolar vessels, and evidence of traumatic pulmonary hemorrhage. A more recent report indicates that the lesions were also found in other organs, including the epicardium of the heart, and very frequently in the large intestine, which, next to the lungs, proved to be the most susceptible to the effects of blast. As a rule, there are no fractures and no external signs of injury.

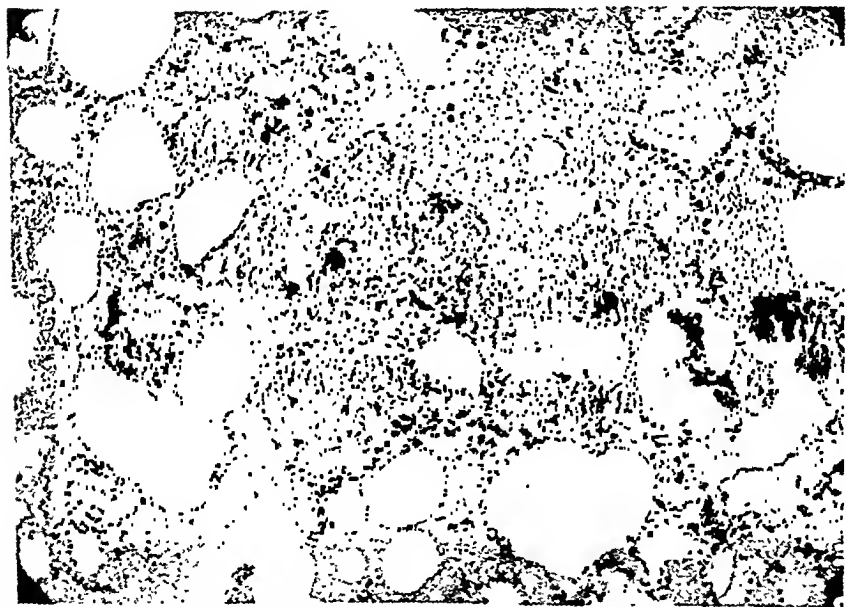


Fig. 3.—Photomicrograph of the lung after injury by contusion in peacetime civilian life. Note the hemorrhagic exudate in the ruptured alveolar spaces.

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chest. A clinical diagnosis of fracture of the skull was made, but *post mortem* examination revealed, besides fracture of the base of the skull, many small hemorrhagic spots scattered over the pleural surface of the lungs, and microscopic examination revealed multiple areas of hemorrhage of varying size scattered throughout the entire lung. Many of the alveoli appeared disrupted and filled with the red blood cells (Fig. 3). This was an instance of peacetime injury of the lung without signs of external chest injury. It was not recognized clinically. The fact that extensive visceral damage can be produced without revealing any external evidence is important from many points of view. The clinical significance of this example is obvious and has been recognized by certain surgeons.

Prophylaxis is possible. This is particularly true of injuries due to high explosives. If one is near an exploding bomb he should attempt to protect his chest from the high pressure wave. This can be done by taking shelter behind a solid object or by throwing oneself face downward into a gutter and letting the pressure wave pass over the curbstone. If there is insufficient time to do more, one should fall flat on his face, since the heavy back muscles and spine afford greater protection to the lungs than the anterior chest wall. It may even be feasible, in the future, to devise some type of protective armor for the chest.

Treatment consists largely in recognition of the existence of such an injury, oxygen therapy, and particularly rest to avoid any additional trauma that might be superimposed upon the already hemorrhagic lung. General anesthesia should be avoided.

REFERENCE

1. King, J. D., and Curtis, G. M.: Lung Injury Due to the Detonation of High Explosive, *Surg., Gynec. and Obst.* 74: 53-62, 1942 (Contains extensive bibliography).
2. Zuckerman, S.: Discussion on the Problem of Blast Injury, *Proc. Roy. Soc. Med.* 34: 171-188, 1941.

FAMILIAL HEMOLYTIC JAUNDICE

A STUDY OF THE RESULTS OF SURGICAL THERAPY

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FAMILIAL hemolytic jaundice has been recognized as a clinical entity since 1900, when Minkowsky¹ published the first accurate description of the condition. The essential diagnostic features of increased fragility of the red blood cells, reticulocytosis, acholuric jaundice, and splenomegalia are now well recognized.

During the past five years, a series of thirty cases of familial hemolytic jaundice have been studied. In sixteen cases, splenectomy was advised because of clinical and laboratory evidence that the disease process was not latent. Thirteen patients accepted this advice and have successfully undergone splenectomy. These thirteen patients, coming from nine distinct and unrelated families, form the basis of this report.

The average age of this group of patients was 25 years, the oldest being 40 and the youngest 5 (Table I). Females predominated in the ratio of 2:1. A definite family history of hemolytic jaundice was obtained in all but two cases in this series. One exception was a boy, 11 years of age, from the Child Saving Institute and repeated efforts to trace his parents were unsuccessful. Definite clinical icterus was present in twelve cases, or 93 per cent of the group, on admission. One patient exhibited only a sallow complexion and muddy sclera, but definite jaundice was absent.

The presenting symptoms in this group of patients subjected to splenectomy are listed in Table II. It is of interest that weakness, fatigue, and jaundice were the outstanding complaints in all but two of the series as evidence of the constant blood destruction with associated icterus.

Pain in the left upper quadrant was noted in those who were experiencing a sudden exacerbation of the hemolytic factor with associated enlargement of the spleen. Fever, chills, nausea and vomiting, likewise, were attendant symptoms in those admitted during a more active phase of the disease.

The spleen was readily palpable in each of the thirteen cases. In five instances, the organ extended from two or four fingerbreadths below the left costal margin, in five, to the level of the umbilicus, and in three instances the mass reached the anterior superior spine inferiorly and extended medially past the midline.

The principal complications of familial hemolytic jaundice are noted in Table III. Of these complications, acute hemolytic crises, or "crises of deglobulization" are the most interesting and important. The exact

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TABLE I
SERIES OF THIRTEEN CASES

Average age	25 years
Oldest age	40 years
Youngest age	5 years
Males	5 cases
Females	8 cases
Family history	85%
Icterus present	93%
Spleen palpable	100%

TABLE II
ADMISSION COMPLAINTS AND ORDER OF FREQUENCY

COMPLAINT	NUMBER OF CASES	PER CENT
Weakness	11	83
Fatigue	11	83
Jaundice (mild)	11	83
Jaundice (deep)	1	8.5
Splenic mass	6	46
Pain (left upper quadrant)	4	33.2
Pain (right upper quadrant)	3	25
Fever and chills	3	25
Nausea and vomiting	2	17

TABLE III
COMPLICATIONS

Acute hemolytic crisis
Biliary complications
Gallstones, cholecystitis
Calculous common duct obstruction

precipitating factor for these acute hemolytic crises has never been determined, and a careful study of this series of patients offers no adequate explanation. The tendency for several affected members in a family to experience these episodes within a period of a few days' time has been one of the most interesting features of this disease. In one of these families a mother and her daughter, aged five years, both developed acute hemolytic crises within one week, reducing their red counts to levels below 1,000,000. In a second family, a girl and her two brothers took gravely ill with typical crises at the same time. One brother succumbed, one recovered but remains below par with icterus and splenomegalia, and the third reported subsequently for splenectomy with clinical cure.

Cowen,² Scott,³ and Dawson⁴ have all emphasized the seriousness of these acute hemolytic episodes. Patients who have once had a crisis tend to have others and we feel that such a history provides a definite indication for advising splenectomy. A young man, aged 29 years, was observed at the University Hospital five years ago in an acute hemolytic crisis for which splenectomy was advised and refused. X-ray therapy

in large doses was given over the splenic area on several occasions without benefit. He succumbed two years later at his home as a result of a subsequent crisis.

In this series of thirteen splenectomized patients, five, or 31 per cent, gave a history of one or more crises before admission, and two patients were admitted to the hospital during their first acute episode of hemolysis. Neither of these latter two patients was operated upon as an emergency, as advocated by Curtis and co-workers,⁵ but came to splenectomy after the blood picture was somewhat restored by medical means. However, we are fully in agreement with his thought on these cases and believe that emergency splenectomy for acute hemoclastic crises is a logical procedure.

It is now rather generally appreciated that one should not give transfusions to patients suffering with familial hemolytic jaundice before splenectomy, even though the degree of anemia be very striking. Severe reactions are very prone to occur in spite of accurate cross matching of blood, with a sudden and alarming increase in hemolysis of red cells and a further drop in the blood picture. Jones⁶ reports the development of transfusion reactions in 45 per cent of his series of patients who were given transfusions prior to splenectomy. Transfusions were given in two of our early cases before removal of the spleen with a severe reaction in one instance. We now believe that the preoperative administration of blood to these patients is contraindicated, but transfusion may be carried out with complete safety and without fear of a reaction as soon as the splenic pedicle is ligated.

It is generally conceded that biliary complications will develop in approximately 70 per cent of the cases of familial hemolytic jaundice. Naturally, the incidence will be higher in those patients who have been subjected to a chronic hemolytic factor over a period of years, but youth is no assurance that stones will not be present. Rassieur,⁷ in 1937, reported three children in one family under the age of 10 in each of whom gallstones were present at the time of splenectomy for familial hemolytic jaundice (Table IV). None of the group of thirteen patients had been subjected to previous biliary surgery, although two other patients with familial hemolytic jaundice have been observed who had previously undergone cholecystectomy without relief of symptoms and subsequently refused splenectomy. Pemberton⁸ reports that 20 per cent of the patients in his series of cases had previously been operated upon for lesions of the biliary system without the underlying condition being recognized. Cholecystograms were made in ten of the thirteen cases, demonstrating a pathologic gall bladder in six instances. At the time of splenectomy, stones were palpable in six cases, or 46 per cent, of this series.

The management of the associated biliary disease in these patients may present a very difficult clinical problem. The role of the spleen

in familial hemolytic jaundice and clinical experience indicates that the spleen, which is primarily at fault, should be removed first and associated biliary pathology either dealt with at the same time or at some future date. When there is a history of previous biliary colic and stones are palpable when splenectomy is undertaken, one's natural desire is to deal with the spleen and the gall bladder at the same time. Technically, however, this is often impossible or definitely contraindicated. In one of our cases a cholecystotomy was done at the time of splenectomy with a satisfactory result to date. In four others, secondary cholecystectomy was performed for persistent biliary symptoms. Calculous common duet obstruction, associated with an acute hemoclastic crisis, occurred in one patient in this series. Jaundice of both a hemolytic and obstructive character was intense, with an icterus index of 360 and a rapidly falling blood picture. In this type of patient vitamin K has proved to be of tremendous value since it permits one to attack the spleen safely as a primary procedure with subsequent correction of the biliary pathology. This patient, with adequate preparation by means of glucose and vitamin K, was splenectomized and three weeks later was subjected to cholecystectomy and choledochostomy. He made an excellent recovery and is now back at full-time work without complaints.

TABLE IV
BILIARY COMPLICATIONS

	CASES	PER CENT
Previous gall bladder symptoms	3	23
Previous biliary surgery	0	0
Cholecystograms, done in ten cases		
Pathologic gall bladder	6	46
Gall bladder reported normal	4	31
Obstructive jaundice, on admission	1	8
Gallstones palpable at operation	6	46
Biliary surgery with splenectomy	1	8
Subsequent biliary surgery	4	31

The average blood values for this series of cases are shown in Table V. The sudden and striking increase in the cellular elements of the blood during the course of splenectomy is one of the most interesting features of this condition. Blood studies, in part previously reported,^{9, 10} made at frequent intervals during operation and throughout the postoperative period confirm the observations of Glover and Fargo,¹¹ and Doan and his co-workers.¹² In this series of patients, there was a uniform rise in the hemoglobin during operation and in the hour following, which averaged 23.2 per cent for the group. The erythrocyte counts correspondingly arose during the same period with an average increase of 1,100,000 cells. Both the hemoglobin and erythrocyte readings then gradually fell during the next forty-eight hours to approach the preoperative readings. A gradual increase then appeared in both readings with normal counts in almost every case at the end of the first postoperative month.

The leucocyte counts also became elevated during splenic manipulation, averaging 28,000 one hour after splenectomy and 46,000 eight hours after operation. This leucocytosis gradually decreased during the post-operative period although a mild elevation of the white cell count, ranging from 10,000 to 15,000, was present in each instance at the time of dismissal.

TABLE V
BLOOD PICTURE IN SERIES OF THIRTEEN CASES

	HB	R.B.C.	RETICU- LOCYTES	ICTERUS INDEX	PLATELETS
Average admission	61	3,300,000	12.3	57	203,000
Low	20	930,000	4	5	156,000
High	98	5,400,000	31	360	240,000
Average dismissal	84	4,700,000	1.8	9	334,000
Low	69	3,870,000	.2	3	209,000
High	107	5,600,000	7	22	480,000

These immediate and dramatic changes in the blood picture are characteristic of the patient with familial hemolytic jaundice during and following splenectomy. They have not been observed in five patients with atypical hemolytic jaundice subjected to splenectomy, nor were they again noted in the four patients who were subsequently subjected to biliary surgery. The probable explanation is a sudden outpouring of cells into the peripheral circulation from an enlarged splenic reservoir that is compressed and manipulated during the surgical procedure. These changes in the blood picture coincide with the reduction in the size of the spleen which occurs during operation and is both visible and obvious. This initial autotransfusion is the factor which permits successful splenectomy in the presence of profound anemia or a crisis without resorting to transfusions. Following splenectomy, transfusion is entirely safe but is rarely necessary; it was employed only once in this series of thirteen cases.

Technically splenectomy in familial hemolytic jaundice is made difficult only by the size of the spleen encountered (Table VI). The average splenic weight in this series of cases was 835 Gm., representing an enlargement of five times the normal size. A few adhesions were present in three instances as a result of previous splenic infarcts with perisplenitis. In only one case did they offer any technical problem. There has been no recurrence of the hemolytic factor in any of this series of cases following splenectomy. When evidence of hemolysis does reappear following removal of the spleen, it may be assumed that (1) the original diagnosis was incorrect, (2) overlooked splenic tissue has become active, or (3) hemolymph nodes have hypertrophied and assumed a hemolytic character.

The essential clinical and laboratory features of familial hemolytic jaundice are now so well established that few errors in diagnosis occur. Furthermore, experience indicates that the autotransfusion reaction ac-

accompanying splenectomy in familial hemolytic jaundice is a typical and essential reaction which occurs in all cases and confirms the diagnosis. As previously noted, the phenomenon of autotransfusion did not occur with splenectomy in five patients with atypical hemolytic anemia, in none of whom was there any permanent benefit from surgical therapy.

The importance of the accessory spleen has been emphasized by Curtis and White.¹³ They reported their presence in 10 per cent of autopsy material studied and in 20 per cent of their cases of familial hemolytic jaundice coming to operation. A careful search was made in each of these thirteen cases and definite accessory spleens were found in three instances, or 24 per cent of the group. In each patient, these accessory splenuli were found in, or taking their attachment from, the principal pedicle of the spleen.



Fig. 1—Spleen with two accessory spleens removed from boy, aged 23 years, with familial hemolytic jaundice, one accessory spleen was attached to the splenic pedicle while the second lay adjacent to the upper pole of the left kidney

Hypertrophy of hemolymph tissue with an assumption of hemolytic characteristics offers a possible explanation for recurrence of symptoms following splenectomy. While this occurs only rarely and is by no means as frequent a cause of recurrence as overlooked accessory splenic tissue, the possibility must always be considered.

We have observed one patient who remained well for two years after splenectomy for hemolytic jaundice and then again developed profound anemia. He received a total of ninety transfusions during the five-year period he survived after recurrence of symptoms. At autopsy there was a striking enlargement of all the abdominal hemolymph nodes, ranging in size from 1 to 3 cm. in diameter. No accessory splenic tissue was found by the pathologist in spite of a very careful search.

TABLE VI
THE SPLEEN IN THIRTEEN CASES

Average weight	835 Gm.
Largest	2200 Gm.
Smallest	300 Gm.
Accessory spleens	3 Cases
Adhesions	3 Cases

SUMMARY AND CONCLUSIONS

A series of thirteen typical cases of familial hemolytic jaundice submitted to splenectomy with clinical cure have been presented. Acute hemoclastic crises and biliary disease were the principal complications encountered. The autotransfusion reaction occurring with the splenectomy in each instance has been discussed and its value in confirming the diagnosis emphasized. Transfusion before splenectomy is definitely contraindicated but may be carried out subsequently without risk. The possible causes of a recurrence of the hemolytic factor in these patients following splenectomy are misdiagnosis, overlooked accessory splenic tissue, or hemolymph tissue which has assumed a hemolytic character.

REFERENCES

1. Minkowsky, O.: Weber eine hereditäre, uten dem bilde eines Chronischen Icterus mit Urobilinurie, Splenomegalia, etc., Verhandl. A. Kongr. q. inn. Med. Weishaden 18: 316-318, 1900.
2. Cowen, S. O.: The Treatment of Familial Acholuric Jaundice, M. J. Australia 1: 265, 1936.
3. Scott, A. M.: Acholuric Jaundice—The Serial Onset of Acute Blood Crises in an Entire Family, Lancet 10: 872, 1935.
4. Dawson, B. E.: Hume Lectures on Hemolytic Icterus, Brit. M. J. 1: 963, 1921.
5. Curtis, G. M., Doan, C. A., and Wiseman, B. K.: Splenectomy for Hemoclastic Crises, Ann. Surg. 104: 892, 1936.
6. Jones, H. W.: The Use of Blood Transfusion in Purpura Hemorrhagica and Acute Hemolytic Jaundice, Ann. Clin. Med. 5: 367, 1926.
7. Rasseur, L.: A Clinical Study of Congenital and Familial Hemolytic Icterus, Tr. West. S. A. 107-121, 1937.
8. Pemberton, J. DeJ.: The Results of Splenectomy in Splenic Anemia, Hemolytic Jaundice and Hemorrhagic Purpura, Ann. Surg. 9: 755, 1931.
9. Shu, W. Jr., and Cunningham, R.: Hemolytic Jaundice—Changes in the Blood After Splenectomy, Arch. Int. Med. 64: 268-279, 1939.
10. McLaughlin, C. W., Jr., Sharpe, J. C., and Cunningham, R.: The Surgical Aspects of Familial Hemolytic Jaundice, New Internat. Clin. 4: 109-127, 1941.
11. Glover, D. M., and Fargo, W. C.: Familial Hemolytic Jaundice, Ohio State M. J. 29: 428-432, 1933.
12. Doan, C. A., Curtis, G. M., and Wiseman, G. K.: The Hemolytopoietic Equilibrium and Emergency Splenectomy, J. A. M. A. 105: 1567-1575, 1935.
13. Curtis, G. M., and White, P. L.: The Surgical Significance of the Accessory Spleen, Tr. West. S. A. 46: 364, 1937.

CHRONIC BILIARY TYPHOID CARRIERS

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SINCE the advent of staunch measures instituted by our public health departments concerning improvement in water supply, better sewage disposal, and sanitary supervision of dairy activity, outbreaks of typhoid fever have become relatively infrequent. The increased use of typhoid vaccine in the civilian population likewise has played a part in lessening the number of people susceptible to this dreaded disease. Nevertheless, there still lurks a great and an actual source of potential danger in the uncontrolled chronic typhoid carrier, and until he is fully recognized and completely managed or cured, epidemic typhoid fever will continue to exist. It is concerning the detection and the treatment of these individuals that this paper deals.

The organism, *Eberthella typhosa*, was first associated with the gall bladder by Anton and Fütterer,¹ in 1888, when they cultured and isolated this bacillus from the gall bladders of fatal cases of typhoid fever. Following their work, later workers in Germany unveiled the fact that the organism could usually be found in the gall bladders of carriers of the disease. Since that time many methods of identifying carriers and many therapeutic agents have been used in the treatment of this condition. Stertenbrink,² in 1928, reviewing the literature on the subject, called attention to the fact that over 100 different therapeutic agents, including laxatives, disinfectants, dyes, vaccines, ultraviolet irradiation, and foreign protein, employed to this date were unsuccessful and unsatisfactory.

Types of Carriers.—A person recovering from either a mild or a severe case of typhoid may soon cease to harbor the organisms or he may continue to excrete them in his urine or feces for a varying period of time. The latter individuals are classed as carriers. There are four places in the human body wherein typhoid bacilli may remain and thus give rise to the carrier state: The urinary bladder, the intestinal mucosa, the biliary radicles of the liver, and the gall bladder. Hepatic, urinary, and intestinal carriers are quite rare and Forsbeck and Hollon³ even cast doubt on the existence of a purely intestinal carrier. Entirely by arbitrary standards, set up by numerous state public health departments, carriers are classed as convalescent or chronic, depending on the length of time they excrete the organisms. Many patients, after an attack of typhosis, harbor the germs in their gall bladders and thus have positive stool cultures for as long as six or eight months. These

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often become spontaneously *Bacillus typhosus* free and are called convalescent carriers. Chronic carriers are only those people who show the presence of the microbes for a year after the infection. In Mississippi⁴ an individual is placed as a permanent or chronic carrier only after at least two positive cultures have been obtained as late as one year after the onset of the disease. Once the term chronic is substituted for convalescent, the person becomes a marked man, for, as Gowen⁵ puts it, once a chronic carrier, always a chronic carrier, unless proper treatment is given.

Perhaps one might argue that as long as there is such a marked decline in the number of cases of typhosus, there must be very few carriers remaining. This is not actually the fact and, instead, carriers are much more prevalent than is realized. In 1936, there were 361 names of carriers on the typhoid registry in the state of New York, exclusive of New York city and state institutions; Stebbins⁶ estimated that, in all probability, the number 5,000 would be nearer the truth. Bigelow and Anderson,⁷ in 1933, found that there were only seventy-five registered carriers in Massachusetts but they thought that the number should be in the vicinity of 1,100. In 1938, a careful survey of the typhoid status in Mississippi was carried out and Gray⁴ estimated from this that there were about 5,991 carriers, or 288 for every 100,000 people, in this state. At the present time in Michigan, we have 275 cases on the typhoid registry but from the above work we can speculate that in reality there should be around 3,600 designated carriers. This number may be somewhat too high but when one considers that from 2 to 4 per cent (Garbat⁸) of all typhoid fever patients become permanent carriers, it is not an impossible one. Most of the recent work (Gray⁴ and Stebbins and Reed⁹) reveals that with modern methods of following typhoid cases for their release, the incidence of the carrier state is one out of every thirty or forty cases, or, roughly between 2 and 3 per cent. An interesting study along these lines was carried out by Stebbins and Reed.⁹ They found the incidence of typhoid fever among household contact of carriers was forty-two times that in the general population, and also that the attack rate among unvaccinated household contacts of carriers was five times that of vaccinated contacts.

Methods of Detection of Carriers.—In order to eliminate and control those unfortunates who are carriers, we must identify them. There are four methods by which this can be and is accomplished. The first and most common is by requiring negative stool and bile specimens for release of all recovered cases; the second is by the routine examination of urine and stool specimens from all food handlers; the third is by epidemiologic investigation of all sporadic cases of typhoid fever; and the fourth is by routine examination of fecal or urine specimens from patients suffering from other illnesses and by culturing of bile from all gall bladders removed by operation.

Felix¹⁰ states that the existence of a carrier in a place where his or her presence is a permanent danger to the community nearly always remains unknown until the outbreak occurs. Numerous recent advances in the bacteriologic approach to the discovery of carriers have been of great aid. Detection is facilitated by the practical application or selective enrichment of culture media as in the selenite F medium of Leifson¹¹ in which the typhoid bacillus multiplies during the first twenty-four hours on incubation while most other intestinal organisms are inhibited. Of even greater value has been the introduction of the bismuth sulfite plating medium of Wilson and Blair,^{12, 13} and the desoxycholate-citrate plate of Leifson.¹⁴ These media inhibit gram-positive bacteria as well as many of the gram-negative intestinal bacilli which always accompany the typhoid organisms in the feces. Mobile diagnostic laboratories to decrease the interval of time between the selection of the specimen and the implantation of it on culture media, are now in use in some states (Gowen⁵). Even with the improved methods, the isolation of typhoid bacilli from feces is a laborious, expensive, and uncertain procedure. There is always the possibility of the intermittency of excretion of typhoid bacilli by the chronic fecal carrier. This chance for error is reduced markedly though, by the use of cathartics, especially magnesium sulfate, and examination of material from the second and third movements.

A new serologic approach to this subject was opened when Felix and Pitt,¹⁵ in 1934, described the Vi antigen of the typhoid bacillus. This antigen is present in all virulent typhoid cultures, hence the designation Vi or virulence antigen. Bhatnager¹⁶ found that during an attack of typhoid fever the Vi antibody appears in the serum at about the same time or somewhat later than the O and H antibodies and persists for a briefer period. According to this author it is demonstrable in all cases of typhosis if the test is made at proper intervals. Felix¹⁰ found that the Vi agglutination reaction is a good test to use as an aid in the detection of chronic typhoid carriers and he strongly recommends it. The frequency of a positive Vi reaction in carriers is high and is independent of the intermittency of bacillary excretion in the feces. For example, one of his patients with an old, apparently healed typhoid empyema who had had a previous rib resection gave a positive Vi agglutination although no bacilli were demonstrably excreted. The use of this procedure is a good way to select probable carriers out of a group of suspects because in some instances, a positive stool culture is obtained only intermittently and then the growth may be very scanty.

Twenty-five strains of *B. typhosus* were isolated from chronic carriers and all of these contained the Vi antigen. The Widal reaction may or may not be positive in chronic carriers but the Vi agglutination reaction is more than 90 per cent accurate according to Felix,¹⁰ Eliot,¹⁷ and Bhatnager.¹⁶ These authors all conclude that the presence of Vi antibody in a person raises the suspicion of some focus of typhoid

infection. Also, the clinically and bacteriologically recovered case, the inoculated person, and the individual with a negative history are alike in that they usually fail to show Vi agglutinins in the blood.

Methods of Treatment.—In 1907, Dehler¹⁸ performed a cholecystostomy and in 1908, Grimme¹⁹ reported a case in which a cholecystectomy was performed for the purpose of curing a carrier. Since this time Grimme's method has become the most generally accepted one and it offers the best chance of cure. In 1935, Gulbrandsen²⁰ reported that four cases of twelve carriers were rendered free of *B. typhosus* by deep roentgen therapy over the gall bladder. Lampe,²¹ in 1937, and Elson and co-workers,²² in 1937, were unable to obtain many cures in their series treated by irradiation. Lyon,²³ in 1932, reported the case of a typhoid carrier who persisted as a carrier following cholecystectomy but who was found to be free of the organisms after a prolonged course of treatment by means of the duodenal tube.

Until 1930, there were no drugs which offered much in the way of satisfactory results in these cases. Onodera, Murakawa and Liu,²⁴ in 1931, reported no growth of *B. typhosus* after twelve to twenty-four hours of exposure to the dye tetraiodophenolphthalein, in 4 to 6 per cent solutions. In cholecystography it is known that a comparable concentration of this dye occurs, for when the concentration reaches 5 to 7 per cent in the gall bladder this organ can be visualized by x-ray. Following this line these observers injected usual doses of dye intravenously in a series of seven typhoid carriers. Of this number, three were free of typhoid bacilli in one month's time but no complete follow-up was apparently carried out. Sangiorgi and di Pierro,²⁵ in 1937, carried out experimental work injecting cultures of *B. typhosus* into laboratory animals and then treated them with iodophthalein. They concluded that this was a possible way of sterilizing the gall bladders of chronic typhoid carriers. Ottenberg,²⁶ in 1933, using a mercury fluorescein derivative, flumerin, cured the carrier state in one out of three patients. He believes it possible to abolish the organisms with flumerin provided that gall bladder is functioning as revealed by cholecystography.

Saphir and Howell,²⁷ in 1940, tried a series of conservative measures, including the use of sulfanilamide, on a carrier of *B. paratyphosus* A, but could not effect a cure. This same patient, given an oral administration of soluble iodophthalein, responded by showing an immediate disappearance of the paratyphoid A organisms from the stool. Repeated stool examinations extending over a seven months' observation period remained consistently negative for these germs. On the other hand, they concluded that the results as to bacteriologic study in vitro concerning the bacteriologic action of the dye on the bacilli of the paratyphosus group did not entirely explain the curative action in a human carrier. In their case they used a dose of 4 Gm. of the dye orally three times in eight days and then once per week for one month.

Enright¹³ recently (1941) reported a case of a typhoid carrier who was treated and apparently cured by the above method, but a complete check on this case has not yet been made.

Saphir¹² and his co-workers studied a large series of typhoid carriers and reported, in 1942, that out of sixty-five individuals treated by means of soluble iodophthalein, the bile was sterilized in twenty-one, or 32.3 per cent, of the cases; however, only five, or 7.6 per cent, of the series were cured of the carrier state. Cutting and Robson,¹⁴ also in 1942, treated six chronic carriers with thionyl, phenothiasine, soluble iodophthalein, sulfaguanidine and sulfadiazine, but obtained no cures. On the other hand, Levi and Willen¹⁵ have a case of a convalescent carrier of five months' duration who was operated upon and a cholecystectomy and appendectomy done. He was not cured by a preoperative trial of iodophthalein and even one month following surgery, his stools were still positive. After a course of sulfaguanidine (0.05 Gm. per kilogram of body weight every eight hours for a week) the stool cultures became negative. Several magnesium sulfate induced diarrhea specimens have also been negative and this patient will probably remain *B. typhosus*-free. This case does not produce positive evidence that sulfaguanidine is of use in the treatment of typhoid carriers because, first, the patient was a convalescent carrier and, second, because he was given the course of the drug only one month following his operation. In many cases the stools became negative if a longer period of time was allowed. On the other hand, though, this case suggests that sulfaguanidine may be an aid in hastening the development of negative stool cultures following cholecystectomy.

Several of our cases have been given from one to four doses of iodophthalein without any change in the carrier state. One of our patients was given 12 Gm. of sulfaguanidine a day for seven days, but the stool culture remained positive. Several others were given an incomplete course of sulfathiazole and sulfanilamide without any change in the carrier status. The possibility that the new group of sulfonamide drugs may have something to offer in the treatment of chronic biliary typhoid carriers should be kept in mind and final judgment reserved until such a time as they have been given an adequate trial.

Relationship of Bile Cultures to the Carrier State.—The importance and necessity of obtaining adequate samples of bile for culture both before and after operation have been stressed by Forsbeck and his co-workers.⁷ Because of the work of Garbat,⁸ who feels that about 15 per cent of carriers, chronic and convalescent, have negative stool cultures, it is urged that all cases have at least one negative bile specimen following cholecystectomy before they are released as cured. In Michigan we have tried to obtain this in every case, but due to various unforeseen difficulties, occasionally it is impossible to obtain postoperative bile specimens. In such cases we have released the carriers with only twelve consecutive negative stool specimens. This should not be

the general practice however. In obtaining the bile specimens, one must remember the points stressed by Forsbeck and Hollon;³ namely, the bile specimen must be clear, amber, viscous, and alkaline, must be obtained following stimulation with magnesium sulfate, and must be protected in buffered broth on its way to the laboratory. Reliance on cultures with a pH below 5 is poor, and cultures of infected bile specimens with a pH of 2 or less after thirty seconds yield no growth. Bile in gastric juice changes color rapidly and hence this characteristic should be recorded immediately. In general, the color changes from blue-green to green, to yellow, to amber, with decreasing acidity of the mixture. Thus, shades of yellow may be satisfactory and amber usually is, for bacteriologic examination.

PRESENT ELIGIBILITY CRITERIA FOR OPERATION AND RELEASE OF CHRONIC BILIARY TYPHOID CARRIERS IN MICHIGAN (COLLER AND CO-WORKERS³⁰)

A. Eligibility criteria for carriers to be operated upon primarily for cure of the carrier state. The person must be:

1. A chronic carrier.
2. A bile carrier.
3. A good surgical risk.

B. Eligibility criteria for release after cholecystectomy.

1. Twelve consecutive feces specimens obtained at monthly intervals following operation and examined in a laboratory approved by the Michigan Department of Health shall be negative.
2. One bile specimen obtained during the year after operation and considered satisfactory for examination by the Michigan Department of Health shall be examined in an approved laboratory and found to be negative.

Results of Cholecystectomy in Michigan Series.—Since the eighteen cases reported by Collier and co-workers,³⁰ in 1937, we have had the opportunity of studying an additional series of twenty-one new chronic biliary typhoid carriers. Before operation, we obtained bile specimens on all but two of the series and of this number, all but one, which was too acid for a satisfactory culture, was reported as positive. In every instance, a culture of bile was taken from the gall bladder at the time of its removal. Also, at least one positive stool culture was obtained from each of the twenty-one cases. Thus, in this series, it was definitely proved that every person was a chronic typhoid carrier of the biliary type. Of this number, all but two were operated upon by members of the University Hospital staff at Ann Arbor. In all of these cases the operation was performed primarily for a cure of the carrier state and not for symptoms of gall bladder disease, though the latter did exist in eleven of the twenty-one cases.

In this series, ages of the patients ranged from 11 to 59 years, with the average being 41 years. There were nine men and twelve women.

TABLE I
TYPHOID CARRIERS TREATED BY CHOLECYSTECTOMY SINCE 1936

	AGE	SEX	YEARS SINCE INFEC- TION	SYMPTOMS	GALL BLADDER PATHOLOGY		X RAY	DIAG- NOSTIC PREOP- ERATIVE BIOPS- ES	BILFS AT OP- ERATION	RFT FASE BILE SPECIMENS	DAYS STOOL S POSITIVE POST- OPERA- TIVE	NUM- BER OF NFGA- TIVES AFTER LAST POST- OPERA- TIVE STOOL	RESULT
					CHRONIC INFECTION	STONES							
1. R D	11	T	5	None	Slight	Yes	None	None	Pos.	None	13	15	Cured
2. G G.	19	M	3	None	Severe active chronic infection	Yes	Faintly visible	Pos.	Pos.	None	8	13	Cured
3. R S	22	M	5	None	Moderate	Yes	None	Neg.	Pos.	None	11	3	In doubt
4. M. D.	30	F	2	Pain in RUQ associated with nausea and vomiting	Severe*	Yes	Non visible	Pos	Pos.	2 Neg.	1	16	Cured
5. M A.	30	M	20	None	Moderate	None	None	Pos.	Pos.	2 Neg.	13	13	Cured
6. L. J.	34	M	15	None	Slight	Yes	Non visible	Pos	Pos.	None	16	2	In doubt
7. F P.	35	F	7	None	Moderate	Yes	None	Pos	Pos.	1 Neg.	12	12	Cured
8. A. D.	38	M	1	Intolerance to fats	Moderate	Yes	None	Pos	Pos.	1 Neg.	6	12	Cured
9. E C.	41	F	10	Intolerance to fats	Moderate	None	Non visible	Pos.	Pos.	2 Neg.	8	12	Cured

*Severe active chronic cholecystitis with active tuberculous and pyogenic pericholecystitis
†This patient was a deaf mute released without bile drainage
RUQ, right upper quadrant

No.	C. H.	15	F	27	Intolerance to fats; occasional pain in R.U.Q.	Moderate	Yes	Faintly visible, 1 stone	None	Pos.	None	10	14	Cured
10.														
11.	M. B.	16	F	2	Intolerance to fats; pain in R.U.Q.	Slight	None	None	Pos.	Pos.	None	267	12	Cured
12.	M. K.	16	F	5	Flatulence	Severe	Yes	Non-visible	Pos.	Pos.	1 Neg.	163	13	Cured
13.	F. G.	46	M	26	None	Moderate	Yes	Non-visible	Pos.	Pos.	1 Pos.	800+	None	Not cured
14.	L. J.	17	M	2	Occasional jaundice and pain in R.U.Q.	Severe	None	Faintly visible	Pos.	Pos.	20 Pos.	100+	None	Not cured
15.	V. B.	19	M	7	None	Moderate	Yes	None	Pos.	Pos.	1 Neg.	102	12	Cured
16.	P. R.	19	F	5	Pain in R.U.Q. and occasional jaundice for 1 year	Severe	Yes	Non-visible	Pos.	Pos.	2 Neg.	112	12	Cured
17.	A. G.	51	F	11	None	Moderate	Yes	Non-visible	Pos.	Pos.	2 Neg.	16	14	Cured
18.	J. C.	53	F	7	Pain in R.U.Q. and occasional jaundice for 2 years	Moderate	Yes	Non-visible	Pos.	Pos.	3 Neg.	150	18	Cured
19.	B. M.	51	F	9	Intolerance to fats; pain in R.U.Q.	Severe	Yes	Non-visible	Pos.	Pos.	1 Neg.	13	2	In doubt
20.	C. S.	57	F	2	Intolerance to fats; pain in R.U.Q.	Moderate	None	Non-visible	Pos.	Pos.	None†	8	17	Cured
21.	J. K.	59	M	7	None	Moderate	Yes	Faintly visible	Pos.	Pos.	1 Neg.	34	12	Cured

The average age for the males was 38 years and for the females, 43 years. We were unable to obtain a history of previous typhoid infection in four of these; however, in the remainder, the interval between the infection and the operation varied from one to twenty-seven years, the average being eight and one-half years.

In each instance the gall bladder was examined pathologically after its removal and in every case, evidence of some degree of chronic inflammation was found. Three specimens were designated as showing slight chronic cholecystitis, twelve as moderate, and six as severe, active chronic cholecystitis. The presence of hyperplastic rudimentary lymphoid follicles in the papillae of the gall bladder mucosa, as described first by Mallory and Lawson,³¹ was a very common finding. There were stones found in sixteen, or 76 per cent, of the group. Botsford³² reported a case in which *B. typhosus* was cultured from the center of a gallstone 2 cm. in diameter, removed 43 years after the patient's original attack of typhoid fever.

The study of the function of typhoid gall bladders, as exhibited by their ability to concentrate the dye tetraiodophenolphthalein, is of interest. We obtained preoperative cholecystograms in fourteen of our twenty-one cases. In not a single instance did we obtain a report of normal visualization, although Haussen³³ reported that four out of six cases that he studied showed this. Instead, faint visualization was recorded in four of the patients and nonvisualization in the other ten. Although there was cholelithiasis in ten cases x-rayed, in only one was a stone visualized by cholecystography. If all cases of chronic biliary typhoid carriers fail to concentrate the dye to any greater extent than is shown in this group, one can readily see that a method of treatment as described by Onodera and others²⁴ will have its limitations.

We feel that sixteen of our series are definitely cured of the carrier state, though we do not have release bile specimens on all of them. Three additional patients who have had their operations quite recently, have not been discharged from the hospital long enough for any positive opinion to be formed as to the final result. However, in each of these instances, the first several stool specimens have been negative and we feel that they also will, in time, be classed in the cured group. Omitting these three individuals, then, we have a percentage cure of 88.9 per cent. Considering these other three as cured would only tend to raise the above percentage to 90.5 per cent.

Two of our patients are, without a doubt, not cured and probably belong to that small group of carriers in which the biliary radicles of the liver are infected. In both, the postoperative bile specimens were positive. C. J. MacGuire³⁴ reported a case where cholecystectomy failed to cure the carrier state. In this instance reoperation revealed stones which were acting as foci of infection in the common and hepatic ducts. A cure was instituted by removal of the stones and drainage of the

common duct. In one of our two failures, at the time of operation, a choledochostomy was performed but no stones were found. A total of twenty bile specimens was obtained before withdrawal of the T tube from this person ten months later, and all were positive. This man had the infection only two years before operation but his gall bladder was one of the group which showed evidence of very severe active chronic cholecystitis, although it contained no stones. Our other failure had the infection twenty-six years previously and his gall bladder showed chronic cholecystitis as well as the presence of stones. He had no symptoms before operation and it is doubtful if exploration of the common duct would have much to offer in his case.

From an analysis of the reports on the stool cultures obtained after operation in the cured group, we found that there appeared to be two types of chronic biliary typhoid carriers. One in which the gall bladder alone is the focus of infection, the other in which there are apparently smaller additional foci in either the intestinal or biliary tracts. To the former class belong those cases wherein the stool cultures become *B. typhosus*-free soon after operation; eleven of our sixteen cases fall into this category. Here the stool cultures were negative within one to thirty days following cholecystectomy. To the second class we ascribe those cases in which there is a marked delay in obtaining negative stool cultures. The remaining five cured carriers should be classed here. These produced positive cultures from 102 to 267 days following surgery. Apparently, here the additional foci were freed of typhoid bacilli by the powers of the body alone after the major source of the infection, the gall bladder, had been removed. Collier and his co-workers³⁰ reported one case in which the feces became negative and remained so, but not until 308 days following cholecystectomy. In those patients who have persistently positive stool specimens following operation, we suggest a trial of sulfaguanidine or one of the other sulfonamides in the hope that it may hasten the destruction of any remaining typhoid foci within the intestinal tract.

Numerous other authors, namely, Haaland and Haaland,³⁵ Whipple,³⁶ Bigelow and Anderson,⁷ Senftner and Coughlin,³⁷ Deibert,³⁸ and Hanssen³³ have followed the results of cholecystectomy as a method of cure for chronic biliary typhoid carriers. All have reported series of cases and their cures range from 68 to 100 per cent. We feel that our average of 88.9 per cent compares favorably with their figures. In this series of twenty-one cases and also in the previous group of eighteen cases reported in 1937, there have been no fatalities. We feel that this is an important fact to bear in mind, especially when trying to convince a carrier, who has no symptoms, that he should submit to operation. So far as we can determine, there is no way in which one can positively free a person from the carrier state, but cholecystectomy definitely affords the best and most certain method. In addition, the high incidence of gall blad-

der disease and gallstones in this type of case usually makes the procedure a benefit to the patient's general physical condition as well as a blessing to the security of his neighbors.

SUMMARY

1. The carrier state was cured by cholecystectomy in sixteen out of eighteen cases, giving a percentage of 88.9 per cent.
2. If we include three additional apparently cured cases, the value will be raised to 90.5 per cent.
3. The cured cases fall into two groups, one in which the feces become rapidly negative after operation, and the other in which the stools remain positive for a much longer time.
4. No deaths occurred in our twenty-one cases.
5. Cholecystectomy affords the best method of treating the chronic biliary typhoid carriers.

REFERENCES

1. Anton, B., and Futterer, G.: Untersuchungen über Typhus Abdominalis, München. med. Wchnschr. 35: 315-318, 1888.
2. Stertenbrink, A.: Beiträge zur Pathologie und Therapie der Typhusbacillen-träger; kritische Zusammenstellung über die Ergebnisse der medikamentösen Behandlung der Typhus- und Paratyphusbacillienstuhlausscheider, Ergebn. d. inn. Med. u. Kinderh. 33: 143-173, 1928.
3. Forsbeck, F. C., and Hollon, H. E.: Standards for Determining the Suitability of Bile Specimens for Detection or Release of Typhoid Carriers, Am. J. Public Health 27: 253-260, 1937.
4. Gray, A. L.: The Probable Typhoid Carrier Incidence in Mississippi, Am. J. Pub. Health 28: 1415-1419, 1938.
5. Gowen, J. H.: Typhoid Carrier Control in Illinois, Illinois M. J. 73: 38-43, 1938.
6. Stebbins, E. L.: The Detection and Control of Typhoid Carriers. Symposium on the Typhoid Carrier Problem at the New York Postgraduate Hospital, June 6, 1936. (Reference from Hanssen.³³)
7. Bigelow, J. H., and Anderson, G. W.: Cure of Typhoid Carriers, J. A. M. A. 101: 348-352, 1933.
8. Garbat, A. L.: Typhoid Carriers and Typhoid Immunity, New York, 1922, Rockefeller Institute for Medical Research.
9. Stebbins, E. L., and Reed, J.: Carrier-Borne Typhoid Fever in New York State, Am. J. Pub. Health 27: 233-240, 1937.
10. Felix, A.: Detection of Chronic Typhoid Carriers by Agglutination Tests, Lancet 2: 738-741, 1938.
11. Leifson, E.: New Selenite Enrichment Media for Isolation of Typhoid and Para-Typhoid (Salmonella) Bacilli, Am. J. Hyg. 24: 423-432, 1936.
12. Wilson, W. J., and Blair, E. W. MeV.: Use of a Glucose Bismuth Sulfite Iron Medium for the Isolation of B. Typhosus and B. Proteus, J. Hyg. 26: 374-391, 1927.
13. Wilson, W. J., and Blair, E. W. MeV.: Further Experience of the Bismuth Sulphite Media in the Isolation of B. Typhosus and B. Para-Typhosus B From Feces, Sewage, and Water, J. Hyg. 31: 138-161, 1931.
14. Leifson, E.: New Culture Media Based on Sodium Desoxycholate for the Isolation of Intestinal Pathogens and for the Enumeration of Colon Bacilli in Milk and Water, J. Path. & Bact. 40: 581-599, 1935.
15. Felix, A., and Pitt, M.: A New Antigen of B. Typhosus, Its Relation to Virulence, and to Active and Passive Immunization, Lancet 2: 186-191, 1934.
16. Bhatnager, S. S.: Vi Agglutination in the Diagnosis of Typhoid Fever and in the Typhoid Carrier Condition, Brit. M. J. 2: 1192-1195, 1938.
17. Eliot, C. P.: The Vi Agglutination Test as an Aid in the Detection of Chronic Carriers, Am. J. Hyg. 31: 8-15, 1940.
18. Dehler, A.: Zur Behandlung der Typhus Bazillenträger, München. med. Wchnschr. 54: 779, 2134, 1907.

19. Grimme, B.: Ueber die Typhusbacillenträger in den Irrenanstalten, München. med. Wehnschr. 55: 16-19, 1908.
20. Gulbrandsen, L.: Treatment of Chronic Typhoid Carriers, Illinois M. J. 67: 262-266, 1935.
21. Lampe, I.: Personal communication.
22. Elson, K. O., Miller, S. G., Forrester, J. S., and Chamberlain, G. W.: Radiation and Cholecystectomy as Therapeutic Procedures for Typhoid Carriers, Am. J. M. Sc. 194: 466-470, 1937.
23. Lyon, B. B.: Typhoid Hepatopholangeitis, J. A. M. A. 98: 885-886, 1932.
24. Onodera, N., Murakawa, G., and Liu, S.: Über eine neue Behandlung von Typhoid Carriers, Deutsches Arch. f. klin. Med. 171: 503-514, 1931.
25. ro, V.: Tentativi Sperimentali di sterilizzazione dei portatori del B. tifico mediante lo "jodo-tetragnot," Pathologica 29: 426-427, 1937.
26. Ottenberg, R.: Biliary Antiseptics, J. Infect. Dis. 53: 239-244, 1933.
27. Saphir, W., and Howell, K.: Soluble Iodophthalein in Treatment of Carriers of Typhoid-Paratyphoid Group, J. A. M. A. 114: 1988-1990, 1940.
28. Enright, J. R.: Apparent Cure of a Typhoid Carrier With Soluble Iodophthalein, J. A. M. A. 116: 220, 1941.
29. Levi, I. E., and Willen, A.: The Typhoid Carrier State Treated With Sulfaguanidine, J. A. M. A. 116: 2258, 1941.
30. Collier, F. A., Coleman, F. P., and Forsbeck, F. C.: The Surgical Treatment of Chronic Biliary Typhoid Carriers, Ann. Surg. 105: 791-799, 1937.
31. Mallory, I. B., and Lawson, C. M.: Chronic Typhoid Cholecystitis, Am. J. Path. 7: 71-76, 1936.
32. Botsford, T.: Acute Typhoidal Cholecystitis and Cholelithiasis Occurring Forty-Three Years After Typhoid Fever, New England J. Med. 224: 780-799, 1941.
33. Hanssen, E.: The Present Status of the Typhoid Carrier Problem, New York State J. Med. 39: 1347-1351, 1939.
34. MacGuire, C. J.: Acute Cholecystitis in a Bacillus Typhosus Carrier, Ann. Surg. 108: 783-784, 1938.
35. Haaland, M., and Haaland, M.: Typhoid Carriers in Western Norway; Results of Cholecystectomy, Lancet 2: 1172-1174, 1927.
36. Whipple, A. O.: Surgical Treatment of Bile Carriers, Ann. Surg. 90: 631-642, 1929.
37. Senftner, H. F., and Coughlin, F. E.: Typhoid Carriers in New York State, Special Reference to Gall Bladder Operations, Am. J. Hyg. 17: 711-723, 1933.
38. Deibert, I. E.: Cholecystectomy in Typhoid Carriers. (Reference from Hanssen.³³)
39. Saphir, W., Baer, W. H., and Plotke, F.: The Typhoid Carrier Problem, J. A. M. A. 118: 964-967, 1942.
40. Cutting, W. C., and Robson, G. B.: Alleged Efficiency of Medicinal Treatment of Typhoid Carriers, J. A. M. A. 118: 1447-1449, 1942.

CLINICAL EXPERIENCE WITH SODIUM CHLORIDE REPLACEMENT

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THE importance of restoring sodium chloride to patients who have lost appreciable amounts of that substance requires no further emphasis, and all recent efforts have been directed toward its administration according to the needs of the individual patient rather than by routine orders. In previous publications,¹⁻⁴ simple rules designed to assist one in administering parenteral fluids to surgical patients have been presented. They are as follows:

1. To *restore* sodium chloride lost prior to hospitalization, give 0.5 Gm. of salt per kilogram of body weight for each 100 mg. that the plasma chloride level needs to be raised to reach the normal of 560 mg. per cent.

2. To *maintain* the normal sodium chloride level while abnormal gastrointestinal fluid losses are occurring, give a volume of Ringer's or physiologic saline solution equal to the volume of gastrointestinal fluid lost. If gastrointestinal suction-drainage is instituted, 1000 c.c. of Ringer's solution should be given during the first day to prevent an initial depletion of body electrolytes. Thereafter, follow the volume-for-volume replacement, but a minimum of 500 c.c. of Ringer's solution should be given each day of such drainage, although the gastrointestinal fluid loss may be less than that amount.

Since these rules were published, we have had an additional period of experience with their practical application. It is the purpose of this paper to present the results of this experience.

The twenty-three patients studied were admitted to the hospital with depleted body electrolytes, most commonly as a result of vomiting. Their initial weight, plasma chloride value, carbon dioxide combining power, and in some instances, other blood chemistry studies, were determined shortly after admission. Ringer's solution for replacement of the sodium chloride lost prior to hospitalization was administered according to the clinical rule of giving "0.5 Gm. of salt per kilogram of body weight for each 100 mg. that the plasma chloride level needed to be raised to reach the normal of 560 mg. per cent." Gastrointestinal fluid losses while in the hospital were compensated for by daily administration of Ringer's solution according to the "volume-for-volume" rule. The patients were then followed with daily determinations of body weight, of plasma and urine chlorides, of plasma carbon-dioxide combining powers, and of any abnormal fluid loss.

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It has been pointed out³ that since the surgeon is generally dealing with upper gastrointestinal tract losses, the chloride loss is practically always greater than the sodium loss, hence the use of this plasma chloride level as an index for the replacement of both these ions is reasonable for the great majority of surgical patients.

As in our previous studies on sodium chloride replacement,^{3, 4} it was soon apparent from the results, that these patients fell into two group patterns. First were those of good or fair general condition, whose illness was of relatively recent origin, a few days to three weeks, and whose electrolyte deficiency had resulted from recent or acute upper gastrointestinal tract fluid losses. The second group was made up of patients who suffered from a more prolonged type of illness with consequent poor general condition and lowered electrolytes because of a chronic dietary salt deficiency or gastrointestinal tract fluid loss.

The results of administering Ringer's solution according to the clinical rules to the patients of good or fair general condition are shown in Table I, and they were satisfactory in eleven of the thirteen cases. The plasma chlorides approached the normal value, there was no undue gain in weight, no development of edema or excessive urinary chloride excretion. While the plasma chlorides did not always reach the normal plasma chloride level of 560 mg. per cent, they were above 520 mg. per cent in the majority of cases. It should be more generally realized that the normal value of 560 mg. per cent cannot be reached during many acute illnesses, and that a value above 500 mg. per cent is a satisfactory level for many seriously ill patients and should never be a cause for great concern. The most unsatisfactory result in Table I, that of patient 35, shows a lower plasma chloride at the end of the study than on admission. The facts reveal where the administered salt went. More than one-half of it was excreted in the urine and much was retained with water in the body, the retention being shown by the fact that the patient kept up his body weight for the eight days of the study, while he should have lost 3 to 4 kg. because of an insufficient caloric intake. The patient's plasma proteins were normal and no explanation is offered as to why this abnormal handling of the salt took place.

In Table II the results are given of administering Ringer's solution, according to the clinical rules, to the patients of poor general condition because of a prolonged illness. These patients often did not have a history of recent, severe vomiting and their lowered plasma chlorides from their history seemed to have resulted from a long-standing or chronic sodium chloride dietary deficiency or loss. Only patient 24 in this group responded in an actually satisfactory manner, the final plasma chloride level being 520 mg. per cent. The remaining six patients showed increasingly unsatisfactory results, there being little or no improvement in their plasma chloride level. Five of the six patients gained weight, patients 10 and 8 retaining water and salt to the point of gen-

TABLE I

DATA* SHOWING GOOD RESULTS OF SALT REPLACEMENT THERAPY IN PATIENTS OF GOOD OR FAIR GENERAL CONDITION

NO.	DIAGNOSIS AND OPERATION	WEIGHT ON AD-MISSION (KG.)	PLASMA CHLORIDE LEVEL ON AD-MISSION (MG./%)	CLINICAL RULE, SODIUM CHLORIDE (GM.)	VOLUME-FOR-VOLUME REPLACEMENT (DAYS)	TIME STUDIED (DAYS)	FINAL PLASMA CHLORIDE LEVEL (MG./%)	FINAL WEIGHT (KG.)	RESPONSE
31	P. O. cholecystogastrostomy; ea. pancreas. Severe vomiting	65.0	360	65.0	7	8	507	64.9	Satisfactory
26	Intestinal obstruction; conservative	65.7	502	19.0	7	8	578	68.6	Satisfactory
16	Cholelithiasis; cholecystectomy	84.2	450	40.8	0	3	569	86.3	Satisfactory
6	Gastrojejunal ulcer; resection	68.0	513	16.0	0	2	569	68.8	Satisfactory
8	Chronic Cholecystitis; cholecystectomy with drainage C. D.	67.3	503	19.9	0	2	558	67.9	Satisfactory
11	Intestinal obstruction; conservative	62.1	405	20.1	1	3	556	62.2	Satisfactory
3	Congenital duodenal obstruction; resection, anastomosis	10.8	282	15.1	6	9	530	11.4	Satisfactory
12	P. O. cholecystectomy and choledochostomy; severe vomiting	40.4	397	37.0	0	4	528	36.5	Satisfactory; shock from electrolyte deficiency quickly relieved
22	Gastric ulcer; partial gastrectomy	56.6	347	58.3	5	7	526	53.4	Satisfactory
34	Perforated duodenal ulcer; drainage subphrenic abscess	45.3	440	27.2	4	5	520	44.9	Satisfactory
42	Intestinal obstruction; conservative	49.9	460	22.5	10	11	515	50.8	Satisfactory
4	Incarcerated femoral hernia. Vomiting two days	38.7	430	24.7	2	6	495	40.7	Unsatisfactory; final plasma chloride level not high enough. Patient gained weight
25	Intestinal obstruction; conservative	62.8	512	18.0	7	8	482	62.1	Unsatisfactory; final plasma chloride level less than on admission. Half NaCl given was excreted in urine

*Pertinent data only given.

TABLE II
DATA* SHOWING UNSATISFACTORY RESULTS OF SALT REPLACEMENT THERAPY IN PATIENTS OF POOR GENERAL CONDITION

No.	DISEASE AND OPERATION	WEIGHT ON AD MISSION (KG.)	PLASMA CHLORIDE LEVEL ON AD MISSION (MG./%)	CLINICAL RULE, SODIUM CHLORIDE (GM.)	VOLUME- FOR- VOLUME REPLACEMENT (DAYS)	TIME STUDIED (DAYS)	FINAL PLASMA CHLORIDE LEVEL (MG./%)	FINAL WEIGHT (KG.)	RESPONSE
21	Bleeding gastric ulcer, glomerular nephritis	53.5	356	53.9	3	4	520	49.9	Satisfactory
17	Subacute perforated gastric ulcer; conservative R	51.8	117	27.8	0	4	492	49.7	Unsatisfactory; final plasma chloride level not high enough
39	Duodenal ulcer; partial gastrectomy	51.7	426	33.3	2	3	489	54.9	Unsatisfactory; final plasma chloride level not high enough and patient gained weight. Total plasma protein 8.4 Gm. %.
7	Subacute bacterial endocarditis	46.6	498	14.4	0	2	446	48.1	Unsatisfactory; Total plasma protein 3.7 Gm. % and patient gained weight
10	Diabetes mellitus, gangrene foot, severe sepsis	67.9	391	57.3	0	4	419	74.4	Unsatisfactory; patient in critical condition. Sodium chloride produced general edema
36	Intussusception; operative correction	47.5	407	36.0	11	12	404	51.8	Unsatisfactory; plasma chloride level not increased and patient gained weight
14	Abdominal carcinomatosis, carcinoma of stomach	55.2	396	45.5	8	9	396	63.5	Unsatisfactory; patient developed general edema. Total plasma protein 4.9 Gm. %

*Pertinent data only given.

TABLE III
FAILURE OF SALT IN EXCESS OF THE CLINICAL RULE TO IMPROVE THE RESULT*

NO.	DIAGNOSIS AND OPERATION	INITIAL SALT THERAPY				ADDITIONAL THERAPY				RESPONSE
		ADMISSION		RESULT		SODIUM CHLORIDE GIVEN (GM.)	RESULT			
		WEIGHT (KG.)	PLASMA CHLORIDE LEVEL (MG./%)	SODIUM CHLORIDE GIVEN (GM.)	WEIGHT (KG.)		PLASMA CHLORIDE LEVEL (MG./%)			
1	Congenital intestinal malro- tation; operative correc- tion	35.5	330	36.8	426	37.5	36.1 22.15 31.0 22.5 30.0	467 421 460 465 467	37.5 37.9 39.0 38.5 36.8	Plasma chloride level never up to normal; patient excreted large amounts sodium chlor- ide in urine
13	Diabetes mellitus, gangrene foot	57.6	432	59.7	505	37.0	16.4	495	60.6	Patient excreted 52 Gm. so- dium chloride in urine
17	Perforated duodenal ulcer; conservative R	51.8	447	49.7	492	27.8	17.0	513	51.4	Patient excreted 9 Gm. so- dium chloride in urine
32	Cancer of the colon	42.4	503	43.6	502	14.4	21.0 18.0	464 505	45.1 50.5	Additional sodium chloride did not improve plasma chloride level; patient de- veloped edema

*Pertinent data only given.

*Pertinent data only given.

eral edema. A low total plasma protein was an important background for the water and salt retention and consequent gain in weight for patients 7 and 18, but water and salt were held by patient 39, whose total plasma proteins were normal. This latter combination has been noted before.^{3, 5, 6} The importance of severe sepsis as a factor setting the stage for edema is shown by patient 10. It is apparent that when the factors establishing the background for the development of edema⁷ are present (general malnutrition, low plasma proteins, sepsis of all types, severe hemorrhage, profuse serous drainage, severe renal or hepatic damage) any amount of salt solution is likely to be handled abnormally, and if the amount called for by the clinical rule is large, as for patients 10 and 18, edema may be expected. In the clinical handling of the sodium chloride needs of the seriously ill group, caution is needed and an unsatisfactory response is not surprising. Before deciding that a patient with low plasma electrolytes and poor general condition from malnutrition and/or sepsis needs a large amount of saline solution, the possibility of a poor response and edema production should be considered and the salt administration accordingly modified.

In the course of this study the question was raised as to whether the patients of poor general condition would have better results if they were given more salt than the amount called for by the clinical rule. From previous experience we thought the reverse would be true, but as a trial, additional salt was given to four patients whose previous response had been unsatisfactory. The data are shown in Table III. The additional salt given was calculated by a reapplication of the clinical rule, using the patients' previous weights and plasma chloride levels. In no instance did the further administration of Ringer's solution appreciably improve the patients' original responses. The plasma chloride levels were not materially increased, and the patients either gained more weight or excreted large amounts of sodium chloride in the urine. It is definitely our impression that the clinical rule for restoring sodium chloride previously lost does supply a sufficient amount, and that the failure of the plasma sodium and chloride level to approach the normal is due to abnormal retention of the salt and water in the body or to the excretion of the salt in the urine. We have observed that if the patient's general condition improves, as by better nutrition or a lessening of sepsis, abnormally retained salt solution shifts, the plasma chloride increases to normal, and excess salt and water are excreted by the kidneys.

SUMMARY

A study was made to determine the value of two simple rules developed for the administration of proper amounts of salt sodium to surgical patients needing water and sodium chloride. It was found that the replacement was satisfactory in the patients of good or fair general condition who had suffered an acute or recent loss of gastrointestinal fluid. Patients who had a more chronic illness and whose general con-

TABLE III
FAILURE OF SALT IN EXCESS OF THE CLINICAL RULE TO IMPROVE THE RESULT*

NO.	DIAGNOSIS AND OPERATION	INITIAL SALT THERAPY					ADDITIONAL THERAPY			RESPONSE
		ADMISSION		SODIUM CHLORIDE GIVEN (GM.)	RESULT		SODIUM CHLORIDE GIVEN (GM.)	RESULT		
		WEIGHT (KG.)	PLASMA CHLORIDE LEVEL, (MG./%)		WEIGHT (KG.)	PLASMA CHLORIDE LEVEL (MG./%)		WEIGHT (KG.)	PLASMA CHLORIDE LEVEL (MG./%)	
1	Congenital intestinal malrotation; operative correction	35.5	330	37.5	36.8	426	36.1 22.15 31.0 22.5 30.0	467 421 460 465 467	37.5 37.9 39.0 38.5 36.8	Plasma chloride level never up to normal; patient excreted large amounts sodium chloride in urine
13	Diabetes mellitus, gangrene foot	57.6	432	37.0	59.7	505	16.4	495	60.6	Patient excreted 22 Gm. sodium chloride in urine
17	Perforated duodenal ulcer; conservative R	51.8	447	27.8	49.7	492	17.0	513	51.4	Patient excreted 9 Gm. sodium chloride in urine
32	Cancer of the colon	42.4	503	14.4	43.6	502	21.0 18.0	464 505	45.1 50.5	Additional sodium chloride did not improve plasma chloride level; patient developed edema

*Pertinent data only given.

*Pertinent data only given.

Plasma chloride level never up to normal; patient excreted large amounts sodium chloride in urine

Patient excreted 22 Gm. sodium chloride in urine

Patient excreted 9 Gm. sodium chloride in urine

Additional sodium chloride did not improve plasma chloride level; patient developed edema

BODY FLUID STUDIES IN EXPERIMENTAL OBSTRUCTION AT VARIOUS LEVELS OF THE GASTROINTESTINAL TRACT*

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THE purpose of this paper is to sum up briefly the changes in body water which occur in dogs after the gastrointestinal tracts have been obstructed at various levels.

When one goes over the vast amount of literature on intestinal obstruction, many views are found as to the presence and the extent of dehydration.¹⁻⁴ Much of the misunderstanding has arisen because of the failure to differentiate shock caused by marked intestinal distension or strangulation, from simple dehydration.³

In our study the plasma volume was measured by means of the Evans blue dye, or T-1824 method, as described by Gregersen and Stewart.⁵ The available fluid, or roughly the extracellular fluid volume, was determined by the sodium thiocyanate method as described by the same authors. In calculating the total amount of circulating plasma protein the plasma volume was multiplied by the protein concentration per cubic centimeter.

The intestines of anesthetized dogs were obstructed by tying a gauze tape securely around the bowel, so as to occlude the lumen, but not tightly enough to produce necrosis. In some instances the animals were allowed food and water. Dehydration and death occurred more rapidly the higher the level of obstruction and the earlier vomiting occurred.

Shortly after control studies were performed pyloric obstruction was produced. Dehydration occurred rapidly, largely owing to the water and electrolyte loss caused by vomiting.

In Fig. 1, the plasma volume and available fluid volume in per cent of normal are shown at various periods of time, in four dogs with pyloric obstruction. The plasma volume after one to three days of obstruction varied from 66 to 86 per cent of normal, and the extracellular fluid volume between 75 and 95 per cent of normal. The figures in the columns represent the actual amount of fluid lost in cubic centimeters. Determinations of the hematocrit, hemoglobin, and plasma protein concentrations were also made, and although they indicated plasma dehydration, they did not reflect the actual loss of the plasma volume. The second part of Fig. 1 shows the changes found in dogs with the upper portion of the jejunum obstructed. The plasma and extracellular fluid volumes show changes which correspond some-

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dition was poor frequently failed to utilize the sodium chloride in a normal fashion, more commonly depositing the salt and water in extravascular compartments and, thus, not increasing their plasma electrolytes to normal. Less frequently, they excrete the salt in the urine. The additional administration of salt to the group in poor general condition was useless, since it simply increased the abnormal responses. To patients with the common factors setting the background for edema (general malnutrition, low plasma proteins, sepsis of all types, severe hemorrhage, profuse serous drainage, severe renal or hepatic damage) more than moderate amounts of saline solution should be given with caution.

REFERENCES

1. Coller, F. A., Bartlett, R. M., Bingham, D. L. C., Maddock, W. G., and Pedersen, B.: The Replacement of Sodium Chloride in Surgical Patients, *Ann. Surg.* 108: 769, 1938.
2. Bartlett, R. M., Bingham, D. L. C., and Pedersen, S.: Salt Balance in Surgical Patients, *SURGERY* 4: 441 and 614, 1938.
3. Coller, F. A., and Maddock, W. G.: Water and Electrolyte Balance, *Surg., Gynec. and Obst.* 70: 340, 1940.
4. Maddock, W. G., and Coller, F. A.: Sodium Chloride Metabolism of Surgical Patients, *Ann. Surg.* 112: 520, 1940.
5. Coller, F. A., Diek, V. S., and Maddock, W. G.: The Maintenance of Normal Water Exchange With Intravenous Fluids, *J. A. M. A.* 107: 1522, 1936.
6. Curphy, W. C., and Orr, T. G.: Edema in Surgical Patients, *Surg., Gynec. and Obst.* 63: 527, 1936.
7. Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema, *Arch. Surg.* 27: 159, 1933.

In Fig. 2 the results are shown when the terminal ileum was obstructed. The plasma volumes ranged between 50 and 95 per cent of normal, and the extracellular volume from 64 to 98 per cent of normal. The greatest measured body water loss exceeded 2,500 c.c. Here again the rate of dehydration was rather slow unless the animals vomited. The first dog represented attempted to eat food and to consume large quantities of water. Abdominal distension and emesis occurred early and the dog died shortly after these studies were obtained. The third dog, on the other hand, took very little food and water. He vomited occasionally during the first three days and then rarely afterward. Following this, he took only small amounts of water and relieved the abdominal distension by eructating gas; thus he dehydrated very slowly. This dog lost a great deal of weight due to starvation, and after an initial rise in the hematocrit, hemoglobin, and total circulating protein levels, these values showed a gradual decrease due to malnutrition. The fourth and fifth dogs were not given food or water, and thus dehydrated slowly.

After observation of the third dog in this series, we decided to study normal animals in which water and food were withheld, thus determining to what extent the restriction of food and water contributed to the dehydration in the obstructed dogs.

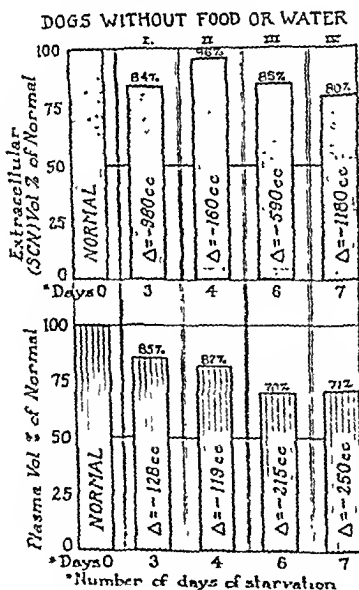


Fig. 3.

Fig. 3 shows the diminished plasma volumes and extracellular fluid volumes in these animals which went without food or water for from three to seven days. The amount of total circulating protein lost over this period of starvation varied between 10 and 32 per cent.

what to the ones seen in the dogs with pyloric obstruction. The first dog received food and water; vomiting occurred more frequently and the animal dehydrated rapidly. The second dog was not given food and water; vomiting did not occur until later and the loss of body fluids occurred slowly.

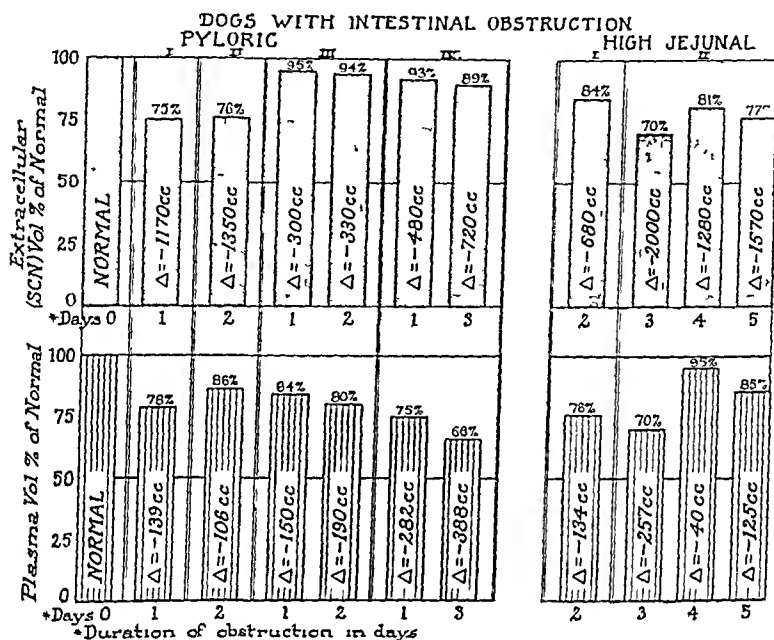


Fig 1

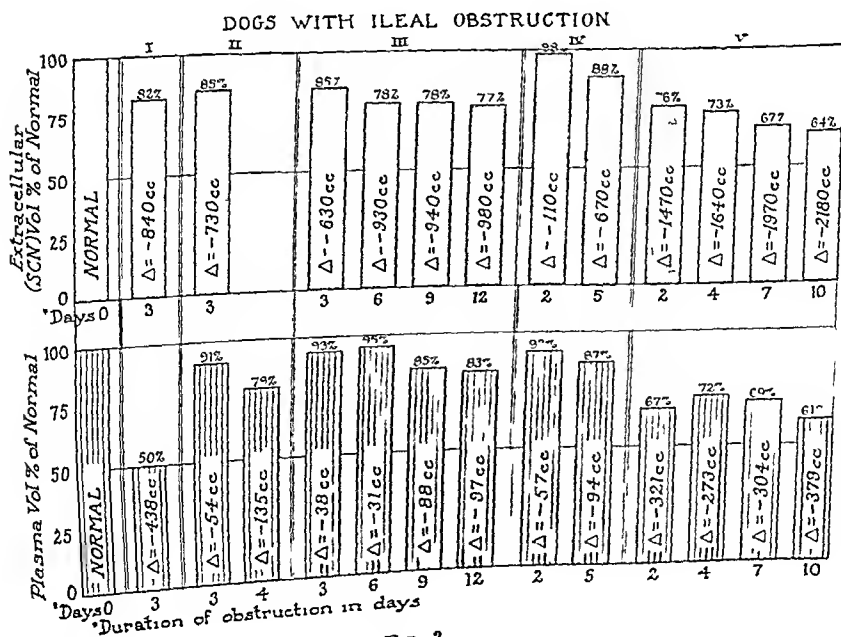


Fig 2

volume associated with peripheral circulatory collapse, which may be superimposed on the already existing dehydration. Thus, a diminished fluid intake, increased fluid loss, and shock, or a combination of all three, might exist. This accounts for the fact that animals and patients show such wide variations in the course of the disease. The rate of development and the severity of the symptoms, thus, depend largely on the amount of food and liquids consumed, the presence or absence of strangulation, the degree of distension and the extent of vomiting, and the level and degree of obstruction.

The hematocrit, hemoglobin, and protein determinations, while they frequently indicate directional changes over short periods of time, cannot be used quantitatively to determine plasma or blood volume changes.

Another important finding which we have also observed in human cases is the diminished total circulating proteins due to malnutrition, even though the hematocrit and protein concentration are normal. Thus, in cases of carcinoma of the stomach we also have observed plasma protein concentrations which were normal, although the total amount of circulating plasma protein was decreased, as much as 45 per cent in one case, because of a diminished plasma volume.⁶

The animals which were allowed to go unchecked until death occurred, all showed the pathologic changes found in shock, which have been well described by Moon and Morgan.⁷ These included hemorrhagic changes in the upper portion of the small intestine, edematous and hemorrhagic lungs, and congestion and hyperemia of the abdominal organs. In none of these experiments was perforation of the intestine with an associated peritonitis present.

REFERENCES

1. Fine, J., Hurwitz, A., and Mark, J.: A Clinical Study of the Plasma Volume in Acute Intestinal Obstruction, *Ann. Surg.* 112: 546-556, 1940.
2. Gendel, S., and Fine, J.: The Effect of Acute Intestinal Obstruction on the Blood and Plasma Volumes, *Ann. Surg.* 110: 25-36, 1939.
3. Foster, W. C.: Acute Intestinal Obstruction, *J. A. M. A.* 91: 1523-1529, 1928.
4. McIver, M. A., and Gamble, J. L.: Body Fluid Changes Due to Upper Intestinal Obstruction, *J. A. M. A.* 91: 1589-1594, 1928.
5. Gregersen, M. L., and Stewart, J. D.: Simultaneous Determination of Plasma Volume With T-1824, and "Available Fluid" Volume With Sodium Thiocyanate, *Am. J. Physiol.* 125: 142-152, 1939.
6. Abbott, W. E., and Mellors, R. C.: Total Circulating Plasma Proteins in Surgical Patients With Dehydration and Malnutrition; Indications for Intravenous Alimentation With Amino Acids, *Arch. Surg.* In press.
7. Moon, V. H., and Morgan, D. R.: Shock: The Mechanism of Death Following Intestinal Obstruction, *Arch. Surg.* 32: 776-788, 1936.

From these experiments, we feel justified in believing that in intestinal obstruction, dehydration might occur due to either insufficient intake of food and water, or to the loss of water and electrolytes.

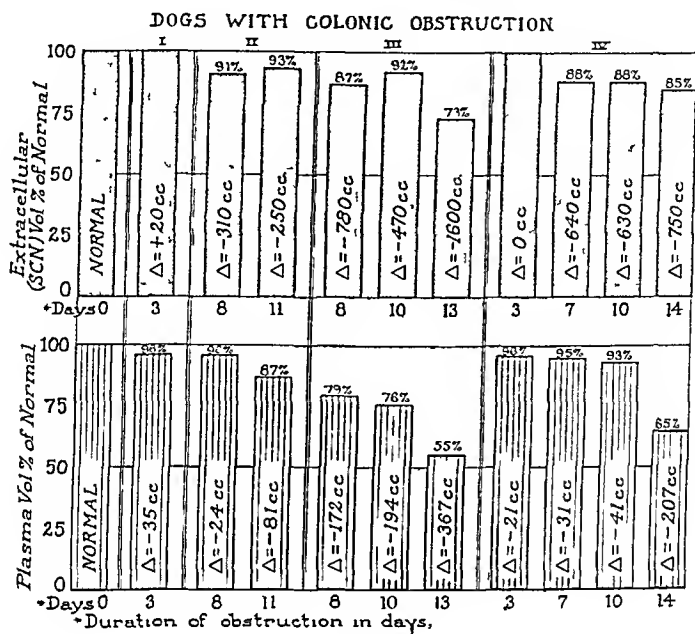


Fig 4

Fig. 4 shows the results on dogs with colonic obstruction, which were allowed food and water. They showed practically no dehydration until after one week. These dogs usually refused food and water after the fourth to the sixth day. They showed a marked weight loss in the second week of illness as a result of malnutrition. The total amount of plasma protein and red cells decreased, although they often showed normal or slightly high concentrations due to a diminished plasma volume. These experiments indicate that severe dehydration may occur if colonic obstruction is present for sufficient time. In the early stage, dehydration progresses as in the starved animal, while later vomiting is superimposed and the rate of body water loss is more precipitous. Clinically, patients with colonic obstruction are not often found to be dehydrated because the obstruction is often partial, and because they usually enter the hospital prior to the time it occurs.

CONCLUSIONS

In summary, we can conclude that experimental intestinal obstruction at any level will produce dehydration, provided the condition exists for sufficient time. In addition, from the observation of others,^{2,3} as well as our own, we believe that marked intestinal distension, or strangulation of an intestinal loop, may cause a rapid lowering of the plasma

which depress or block perception of pain, these agents disturb the physiologic functions of respiration and circulation. Pure drugs of known action, the gift of the pharmacist, could not be used effectively without knowledge of why and how we breathe and why and how the heart beats. Vesalius and Harvey, Boyle and Lower, Priestley and Lavoisier, Bernard and Bert, and a host of modern scientists were necessary. Physiology and pharmacology had to be born. It was necessary to know the effects of drugs on physiologic function. Opium and hyoseyamus were made safe by the acquisition of this knowledge, along with the technical skill in dosage and supervision of respiratory depression.



Fig. 1.—X, external atmosphere; Y, tissue cell; A, respiratory passages; B, respiratory passages; C, capillary and alveolar membranes; D, arterial blood; F, venous blood. (Courtesy of Waters, R. M.: *J. A. M. A.* 115: 1657, 1910.)

In general, we may look upon the cost of comfort as a sacrifice of efficient transport of oxygen to the vital cells of the central nervous system and the removal of carbon dioxide from these cells. Complete interruption of this transport mechanism (Fig. 1) for more than a very few minutes is fatal. Partial interruption can be tolerated for long

MORBIDITY ACCOMPANYING THE THERAPY OF PAIN: THE COST OF COMFORT

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TO STRIVE for the relief of pain was probably one of the earliest efforts and remains one of the most gratifying accomplishments of the medical profession. In all human endeavor, success is attained at a price. Only at a certain cost can misery be transformed into comfort. In the distant past, the cost of comfort often was found to demand too great a sacrifice of safety.

Methods of producing complete oblivion to pain were known in very early times. The *spongia somnifera*^{*} was effective for the relief of pain as used in Italy in the thirteenth century and described by Theodoric in 1297. With only two of its many ingredients, opium and hyoseyamus, we are able to produce adequate surgical anesthesia at the present time. To do so safely in every case requires the best of present knowledge and skill; the former most certainly was not available in the thirteenth century.

The complaint of the German physicians of Paderborn in 1800, that the prescriptions of opium which he prepared for them varied widely in effect, led Fredrie Sertürner, the apothecary's assistant, to discover a method of extracting the active principle of drugs in the form of pure alkaloids. With known and constant drug strength, there remained and still remains the variable of individual susceptibility and the human failing of the erroneously guessed dose and the improperly chosen drug. What is one man's meat is another's poison. Then, even as now, there existed in the soul of the physician the hope that the undesirable depressant effects of drugs which relieve pain might be counteracted by stimulant drugs. Witness the addition of a great number of ingredients to the somniferous sponge with the hope that the sum total effect would relieve the pain and yet retain a safe margin of respiratory exchange. Unhappy results were all too frequent and the sponge fell into disrepute.

To make opium and hyoseyamus safe and yet satisfactory, several contributions were necessary besides the discovery of the soluble salts of the alkaloids, morphine and scopolamine. In common with other drugs

^{*}"Take of opium, of the juice of the unripe mulberry, of hyoseyamus, of the juice of hemlock, of the juice of the leaves of mandragora, of the juice of the woody ivy, of the juice of the forest mulberry, of the seeds of lettuce, of the seeds of the dock which has large round apples, and of the water-hemlock—each an ounce; mix all these in a brazen vessel, and then place in it a new sponge; let the whole boil, as long as the sun lasts on the dog-days, until the sponge consumes it all, and it has boiled away in it." . . . "As oft as there shall be need of it, place this sponge in hot water for an hour, and let it be applied to the nostrils of him who is to be operated on, until he has fallen asleep, and so let the surgery be performed."

in that atmosphere are readily transported to the cells of the body; (2) that any depression of respiration results in a less efficient exchange of that atmosphere, which can only mean suboxygenation and accumulation of carbon dioxide, provided the demand for oxygen and the production of carbon dioxide have not decreased; (3) that any obstruction,

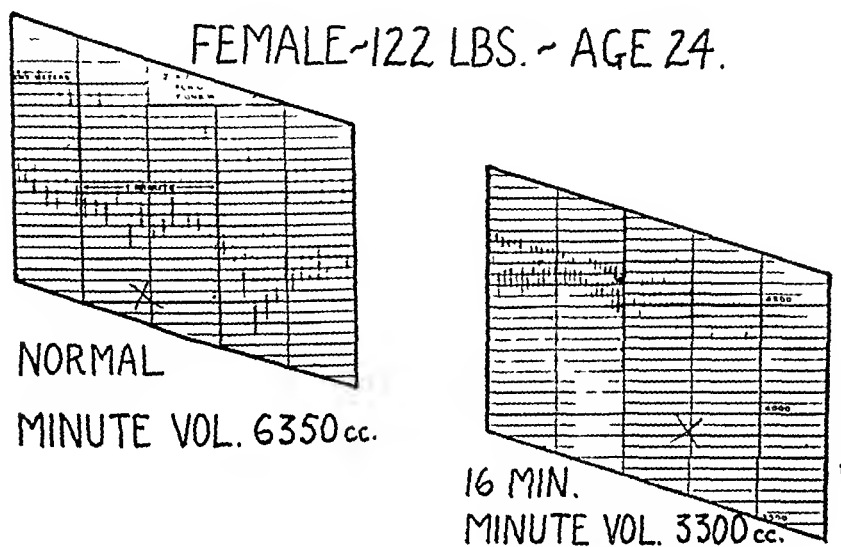


Fig 4—Tribromethanol, 100 mg/kg, administered rectally.

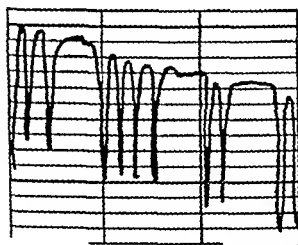


Fig 5



Fig 6

Fig 5—Respiratory tracing one hour after morphine, 1 gr. note the periods of apnea.

Fig 6—Respiratory tracing in the same case twenty minutes after scopolamine, 1/6 gr. No periods of apnea. definite increase in minute volume exchange.

either in the upper respiratory passages where it would hinder free exchange of the atmosphere, or in the alveoli where it would hinder free passage through the alveolar membrane, likewise means suboxygenation and accumulation of carbon dioxide, (4) that any depression of the pharyngeal, laryngeal, and bronchial reflexes which are protective in character will lead to contamination. Jackson has called the glottis

periods without a fatal issue but rarely without temporary or permanent functional impairment. Every physician has learned the workings of this "transport function" in its every detail but too frequently we neglect the application of that knowledge to the everyday care of patients. By observing Fig. 1, several important facts are recalled: (1) that the inhaled atmosphere is separated from the blood stream only by a semipermeable membrane, which means that depressant substances

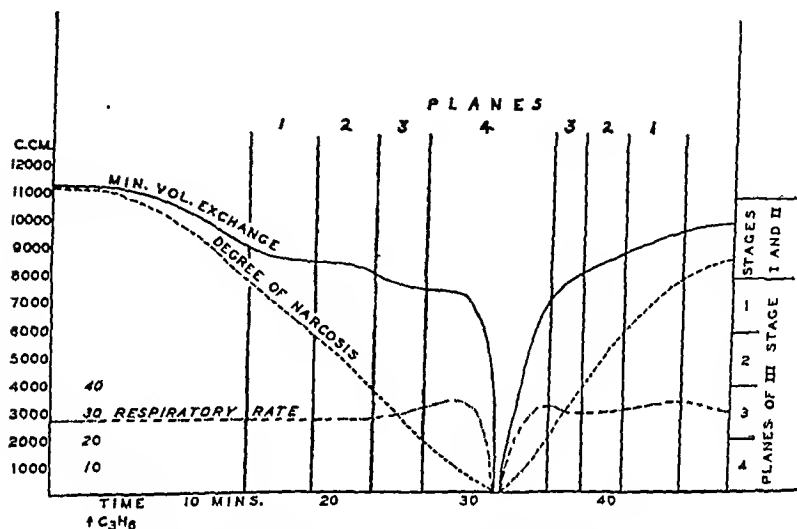


Fig. 2.—Cyclopropane anesthesia; closed carbon dioxide absorption technique (From Waters, R. M. Brit. M. J. 2: 1013, 1936.)

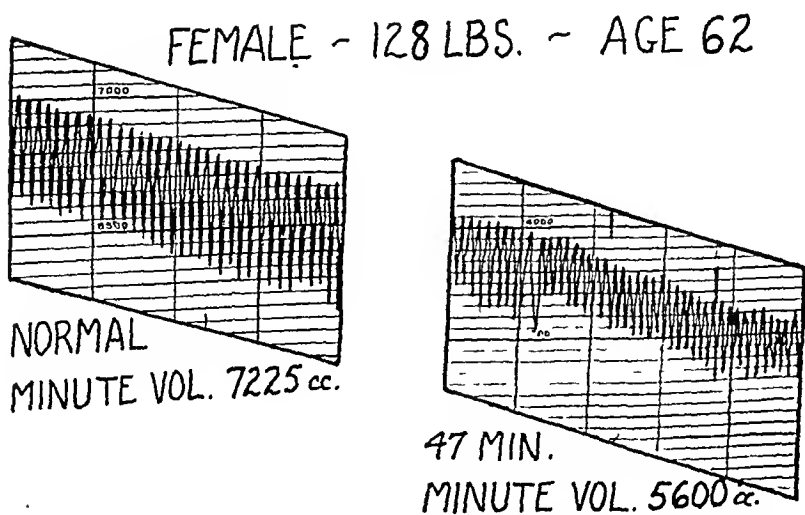


Fig. 3—Sodium pentobarbital, $\frac{1}{4}$ gr., given orally. (From Waters, R. M., and Harris, J. W.: Am. J. Surg. 18: 129, 1919.)

in that atmosphere are readily transported to the cells of the body; (2) that any depression of respiration results in a less efficient exchange of that atmosphere, which can only mean suboxygenation and accumulation of carbon dioxide, provided the demand for oxygen and the production of carbon dioxide have not decreased: (3) that any obstruction,

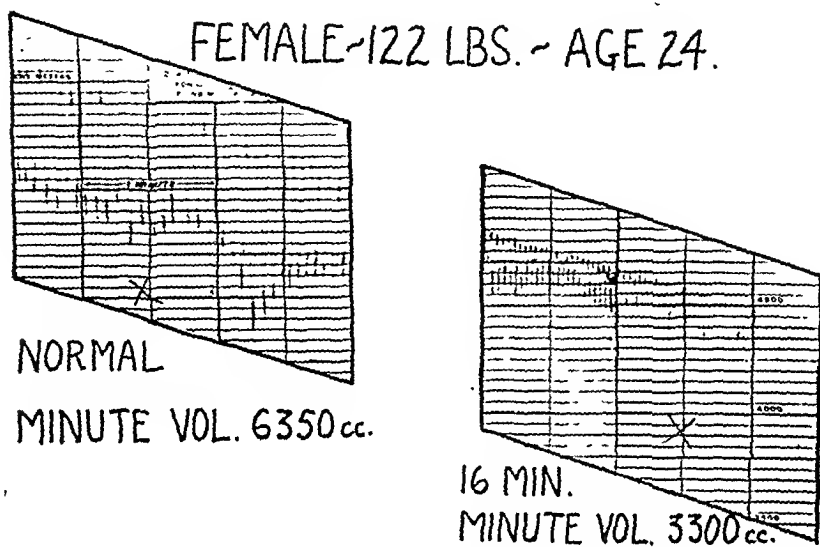


Fig. 4.—Tribromethanol, 100 mg./kg., administered rectally.

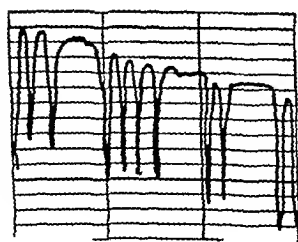


Fig. 5.

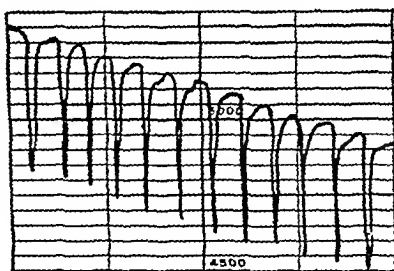


Fig. 6.

Fig. 5.—Respiratory tracing one hour after morphine, $\frac{1}{2}$ gr., note the periods of apnea.

Fig. 6.—Respiratory tracing in the same case twenty minutes after scopolamine, $\frac{1}{20}$ gr. No periods of apnea; definite increase in minute volume exchange.

either in the upper respiratory passages where it would hinder free exchange of the atmosphere, or in the alveoli where it would hinder free passage through the alveolar membrane, likewise means suboxygenation and accumulation of carbon dioxide; (4) that any depression of the pharyngeal, laryngeal, and bronchial reflexes which are protective in character will lead to contamination. Jackson has called the glottis

Hibma and Curreri² have recently made, to the best of our knowledge, the first clinical study of the effect of pain-relieving drugs upon the "janitor service" of the tracheobronchial tree. They found that the combination of morphine sulfate, 0.0162 Gm. ($\frac{1}{4}$ gr.) and atropine sulfate, 0.0013 Gm. ($\frac{1}{50}$ gr.) at the end of one and one-half hours depressed cough and ciliary activity as much as 107 per cent; whereas morphine sulfate, 0.0162 Gm. ($\frac{1}{4}$ gr.) and scopolamine hydrobromide, 0.00064 Gm. ($\frac{1}{100}$ gr.) caused a 62 per cent depression. From these facts, it is understandable why so many patients develop areas of pulmonary

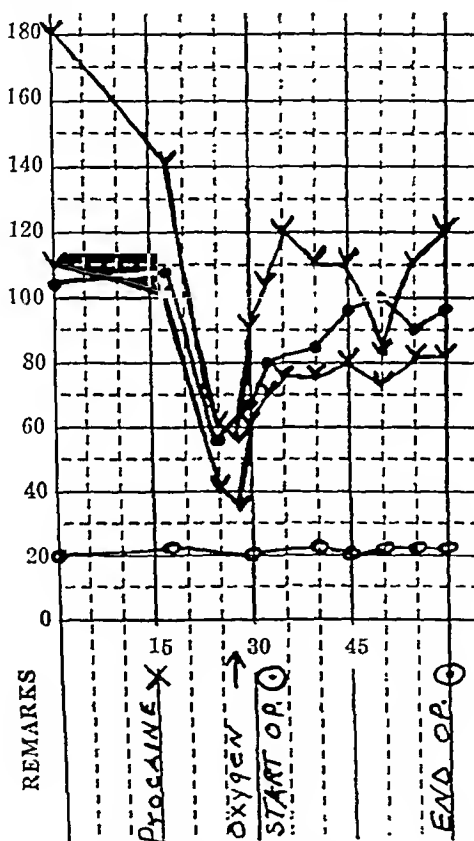


Fig. 8.—Male, aged 64 years. Transurethral prostatic resection; 85 mg., 5 per cent procaine, intrathecally, analgesia to D₁₀

atelectasis which, if not relieved, promote bacterial growth resulting in bronchopneumonia. This is all the more understandable when one remembers that after abdominal operations, almost all patients have tight binders applied and frequently large quantities of air are trapped within the peritoneal cavity, both of which prevent full pulmonary ventilation, and the patient's position is usually not changed frequently enough to prevent the accumulation of secretions.

It has been repeatedly demonstrated by many other clinicians and us that the procedure of tracheobronchial toilet* or the suction removal of secretions through a bronchoscope is very effective in relieving atelectasis if instituted before bacterial invasion has occurred and bronchopneumonia has developed (Fig. 7). When performed with care and skill, neither of these procedures is harmful nor particularly un-

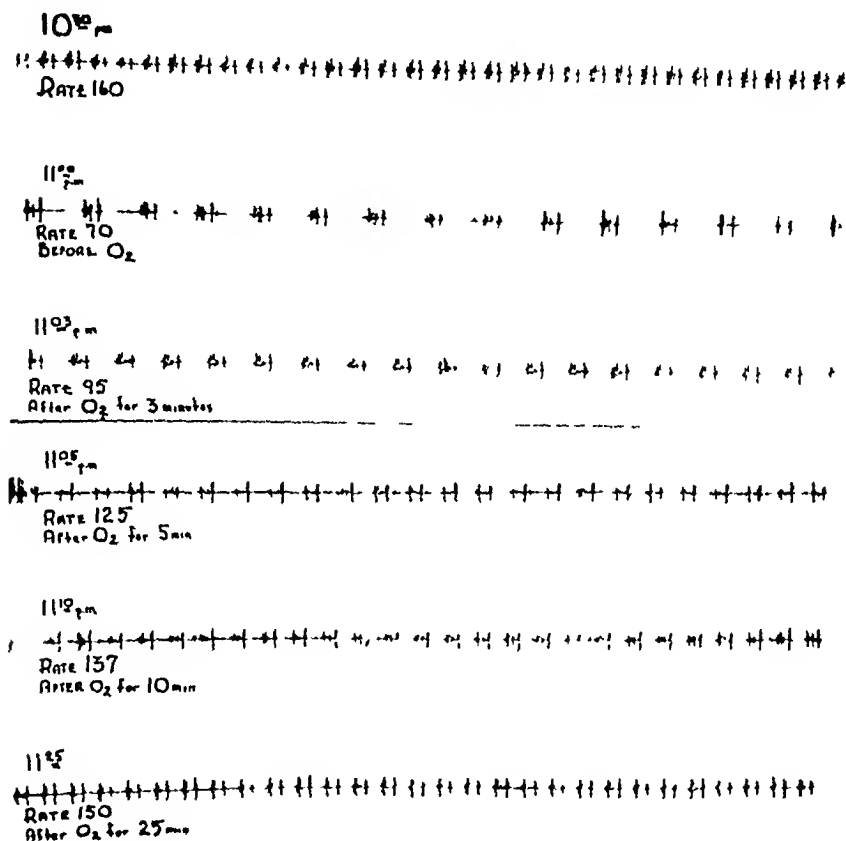


Fig. 9—Changes in the fetal heart rate recorded during a period of suboxygenation of the mother and after restoration

*The details of tracheobronchial toilet should be fully explained to the patient because the success of this procedure depends upon the cooperation of the patient and the skill of the physician. The patient's cooperation is by far the most important. The physician should substitute gentleness for any lack of skill. Local analgesia is obtained by spraying the nares and pharynx with an analgesic solution such as cocaine. A wide bore endotracheal tube well lubricated, is then passed through the nostril as far as the oropharynx. At this point, it is wise to spray the analgesic solution into the tube with inspiration so as to anesthetize the glottis. The tube is now passed through the glottic opening, either on inspiration or expiration. If blind intubation fails, laryngoscopy may be performed and the tube inserted by direct vision. A small rubber catheter well lubricated with vaseline is passed through the tube into the trachea and suction is applied to the catheter. The patient's head should be turned from side to side to direct the catheter into each main bronchus. When be turned from side to side to direct the catheter into each main bronchus. When the trachea and main bronchi appear to be clear of secretions, the patient should be turned first on one side and then the other to promote drainage. It is paramount that the endotracheal tube be as large as can be tolerated so that after the catheter is passed through the tube there is enough space remaining for free breathing. The coughing produced by the irritation of the trachea and bronchi is to be desired, provided it is not too violent.

comfortable to the patient. The tracheobronchial toilet can be performed with local anesthesia and the patient may remain in his own bed.

The cost of comfort cannot be assessed without considering the effects of pain-relieving drugs upon the circulatory system. The functions of respiration and circulation are so closely interrelated in the transport system that one cannot be affected without disturbing the other. Spinal anesthesia is occasionally accompanied by a fall of the systolic pressure with a very small or sometimes indeterminable pulse pressure (Fig. 8). When this degree of circulatory collapse occurs, the resulting mental confusion and the occasional unconsciousness are due to acute oxygen lack

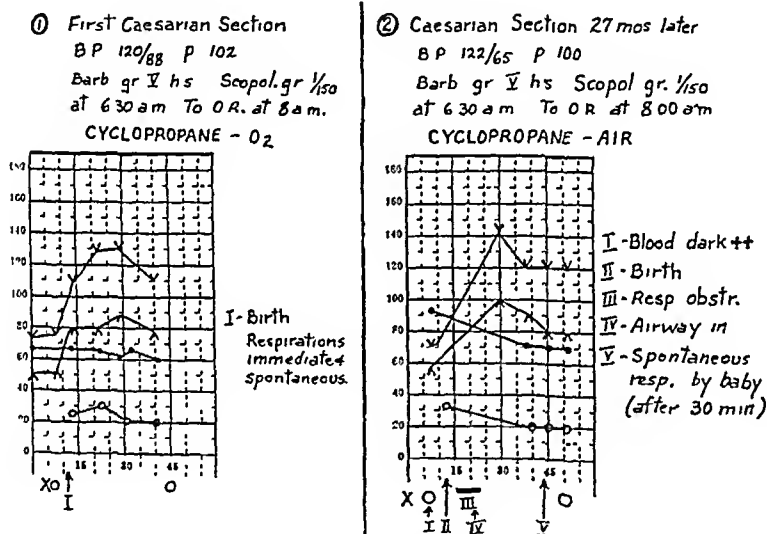


Fig. 10—Records of the same patient anesthetized on two different occasions: (1) Induction with cyclopropane and excess oxygen, (2) Induction with cyclopropane-air mixture and oxygen added later. Acute oxygen want in the mother was transmitted to the baby at the time of birth. (From Waters, R. M., and Harris, J. W. *Am. J. Surg.* 48: 129, 1940.)

of the cells of the higher cerebral centers. Efficient oxygen therapy, if instituted immediately, will usually prevent further circulatory collapse and restore mental acuity to its previous level. The fetal heart is very sensitive to any degree of oxygen lack in the mother (Fig. 9). Note the marked slowing of the fetal heart rate in the second tracing after acute oxygen lack in the mother, with the gradual return to normal as the fetal cells and blood are reoxygenated. As long as the degree of maternal oxygen lack does not reach too great a proportion and as long as oxygen is completely restored, there probably is no great danger to the fetus. The birth should not be allowed to occur before reoxygenation has taken place, but if it occurs accidentally, then asphyxia neonatorum will probably result (Fig. 10).

The coin in which our patients pay for comfort is, with certain exceptions, "deficiency in the functions of the transport system." It is necessary for every physician to provide pain relief for his patients. To deliver this comfort without cost means to maintain the transport system at or near normal with all the knowledge, equipment, and skill at our disposal. Such knowledge, equipment, and skill may prevent, or at worst, bring to a minimum, the morbidity accompanying the therapy of pain and thus reduce the cost of comfort.

REFERENCES

1. Jackson, Chevalier, and Jackson, Chevalier L.: *Bronchoscopy, Esophagoscopy and Gastroscopy*, Edition 3, Philadelphia, 1934, W. B. Saunders Company, p. 410.
2. Wangeman, C. P., and Hawk, M. H.: *The Effects of Morphine, Atropine and Scopolamine on Human Subjects*, *Anesthesiology* 3: 24, 1942.
3. Hibma, O. V., and Curreri, A. R.: *A Study of the Effect of Morphine, Atropine and Scopolamine on the Bronchi*, *Surg., Gynec. & Obst.* 74: 851, 1942.

NONASPHYXIAL NITROUS OXIDE ANESTHESIA

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ONE function of law enforcement agencies is to protect the individual from strangulation. It is an interesting and unfortunate paradox that strangulation under the guise of nitrous oxide anesthesia is all too frequently condoned in the operating room.

In the absence of asphyxia, no pathologic damage can be demonstrated following the use of nitrous oxide.¹ No effort is placed on any organ to detoxify or eliminate the agent and the physiologic mechanisms are left essentially undisturbed. No irritation of the respiratory tract attends its use,² and not least in importance is its nonexplosive character. Under certain conditions, it is highly desirable, if not essential, to use a drug with these properties.

However, because of the false but popular opinion that nitrous oxide anesthesia is necessarily accompanied by asphyxia, its use has been supplanted in some clinics by other agents and techniques. These other agents and techniques may not be as well suited to the patient's condition or as convenient to the surgeon as nitrous oxide properly administered.

PREOPERATIVE MEDICATION

The success or failure of any anesthesia frequently depends upon proper preoperative medication. As a matter of fact, the nonvolatile depressant drugs used preoperatively are actually a part of the anesthesia.

It is imperative that the reflex irritability and metabolic activity be considerably reduced before nitrous oxide or other relatively impotent agents are administered. This is accomplished by the judicious use of depressant drugs preoperatively. The drugs most frequently employed are the short-acting barbiturates, morphine sulfate, and scopolamine hydrobromide. In certain types of cases, avertin has been found to be of value.

The short-acting barbiturates, in amounts usually not exceeding 3 gr. (0.180 Gm.), are given by mouth one-half hour before the morphine and scopolamine. This facilitates the passage of the capsule into the small intestine and favors more complete absorption. Morphine and scopolamine are administered subcutaneously in the ratio of 25:1 one and one-half hours before operation, as recommended by Waters.³ Frequently, because of the estimated reflex irritability and metabolic activity of the

¹Presented at the Second Annual Meeting of the Central Surgical Association, Chicago, Ill., Feb. 27 and 28, 1912.

patient, the total dosage required may exceed morphine, $\frac{1}{4}$ gr. (0.015 Gm.), and scopolamine, $\frac{1}{100}$ gr. (0.0006 Gm.). The dose is then divided into two portions. The first portion, which may be either morphine, $\frac{1}{4}$ gr. (0.015 Gm.), and scopolamine, $\frac{1}{100}$ gr. (0.0006 Gm.), or morphine, $\frac{1}{6}$ gr. (0.010 Gm.), and scopolamine, $\frac{1}{150}$ gr. (0.0004 Gm.), is given subcutaneously two hours preoperatively. After an hour, the patient's response to the drugs is noted and the second portion determined and also administered subcutaneously. This portion is often less but may be equal to the first portion. Usually, it is not necessary, except in cases of greatly increased metabolism, to exceed the total dosage of morphine, $\frac{1}{10}$ gr. (0.024 Gm.), and scopolamine, $\frac{1}{60}$ gr. (0.001 Gm.). Because of age, extreme debility, or other factors, the anesthesiologist frequently desires only partial sedation up to the time of operation and, consequently, orders the first hypodermic given one hour preoperatively and gives the second dose intravenously in the operating room. Accuracy in estimating the amount of drug required and the time at which it is to be given is in direct proportion to the experience and care of the anesthesiologist. It must be emphasized that when relatively large amounts of depressant drugs are used, careful preoperative supervision is absolutely necessary to prevent obstructed airways with resultant anoxia.

After this carefully supervised but simple preparation, surgical anesthesia can be produced and maintained with not over 80 per cent, and frequently as low as 60 or 70 per cent nitrous oxide, without increased pressure. Cyanosis or anoxia are not expected nor permitted and even such low concentrations of nitrous oxide give adequate anesthesia.

It has been held by many that except for its explosive character, the slightly more potent ethylene has most of the desirable characteristics of nitrous oxide. Clinically, we have found that only very rarely can surgical anesthesia be produced with ethylene in concentrations of 80 per cent or less if the premedication is insufficient for nitrous oxide anesthesia.

INDICATIONS

The apprehensive, excitable patient is a better operative and anesthetic risk if adequately sedated. The type of premedication described produces a calm, quiet, and cooperative patient, who usually has several hours' amnesia.

In thyroid disease, especially thyrotoxicosis, this preparation and nitrous oxide anesthesia, if a general anesthesia is to be used, is particularly appreciated by both the surgeon and the patient. From the anesthesiologist's viewpoint, the reduced activity of the carotid sinus reflex, the absence of laryngeal spasm, and the simplicity of the procedure are added factors in its favor.

For operations of considerable length that require little or no relaxation, such as radical mastectomies, vaginal plastics, and multiple excisions of varicosities, nitrous oxide is the least toxic and one of the pleasantest anesthetics that can be chosen.

The anesthesiologist has several agents and techniques in his armamentarium which are suitable for elderly, poor-risk patients, yet none disturbs the physiologic mechanisms less than nitrous oxide. Absence of good relaxation is its only disadvantage. To overcome this disadvantage, regional block used in conjunction with nitrous oxide analgesia has been found to be very satisfactory both from the standpoint of the surgeon and the safety of the patient.

One of the "bugaboos" of the operating room is explosions. In many cases, it is essential to use the cautery or other electrical apparatus such as the bone saw, drill, or x-ray. In spite of the fact that much of the electrical apparatus is supposedly shockproof, it is wiser to employ a nonexplosive agent in its presence. Because of this factor and others previously mentioned, nitrous oxide is of particular value in cases such as the nailing of hips, laminectomies, and spinal fusions.

The satisfactory use of nonasphyxial nitrous oxide anesthesia in thoracoplasties has been previously reported.⁴

POSTOPERATIVE COMPLICATIONS

Upper respiratory and chest complications have been minimal with this method in spite of the fact that it is the anesthesia of choice in most of the poor-risk patients.

Nausea and emesis are slightly more frequent than with cyclopropane and less frequent than with other inhalation agents.

Distention is less, and when it does occur is less severe with nitrous oxide.

SUMMARY AND CONCLUSIONS

Nitrous oxide anesthesia possesses several advantages over other anesthetic agents for certain types of cases. These advantages merit its careful consideration by surgeons and anesthesiologists.

The chief disadvantage is inadequate relaxation.

The only deleterious effects are due to anoxia and not to the drug itself.

Anoxia is not necessary if the patient's reflex irritability and metabolism are adequately reduced by the intelligent use of nonvolatile depressant drugs.

REFERENCES

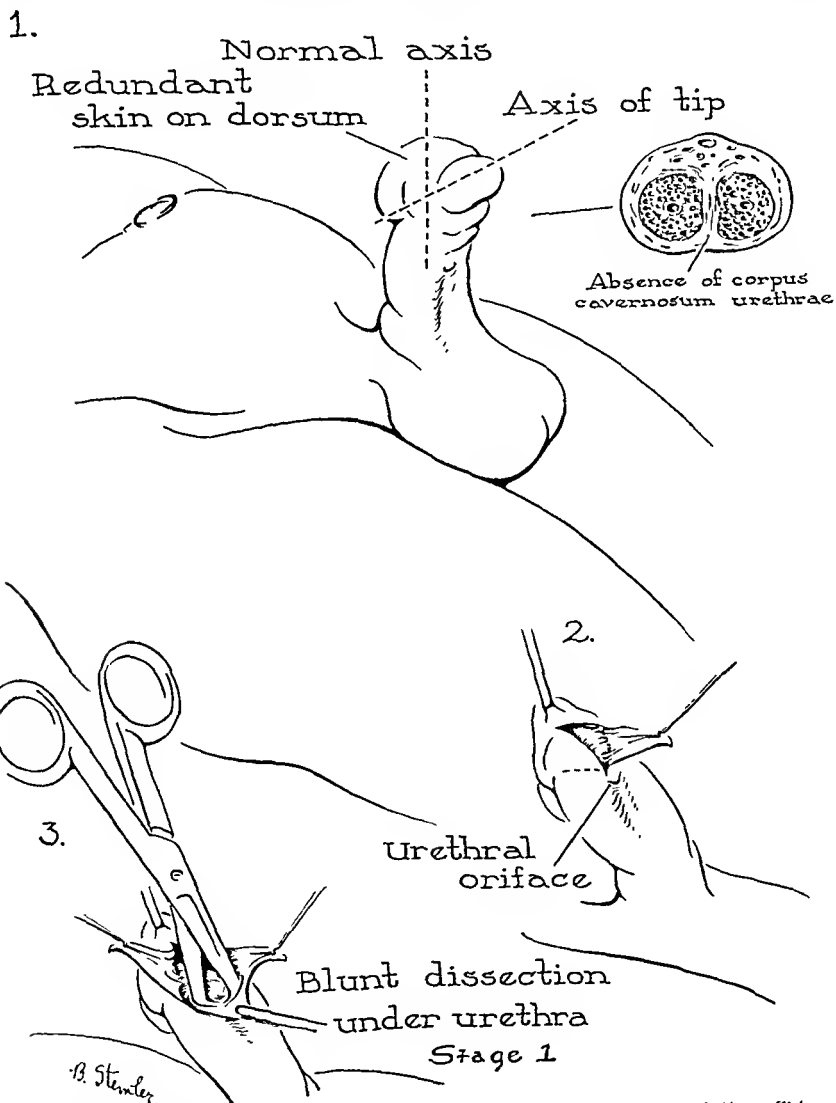
1. Courville, Cyril B.: *Untoward Effects of Nitrous Oxide Anesthesia*, Mountain View, California, 1939, Pacific Press Publishing Association.
2. Seevers, M. H., and Waters, R. M.: *Pharmacology of the Anesthetic Gases*, *Physiol. Rev.* 18: 447-479, 1938.
3. Waters, R. M.: Study of Morphine, Scopolamine and Atropine and Their Relation to Pre operative Medication and Pain Relief, *Texas State J. Med.* 34: 304-305, 1938.
4. Cullen, Stuart C., McQuiston, W. Otis, and Petersen, Vernon W.: Nitrous Oxide Anesthesia for Thoracoplasty, *Anesthesiology* 2: 310-316, 1941.

HYPOSPADIAS

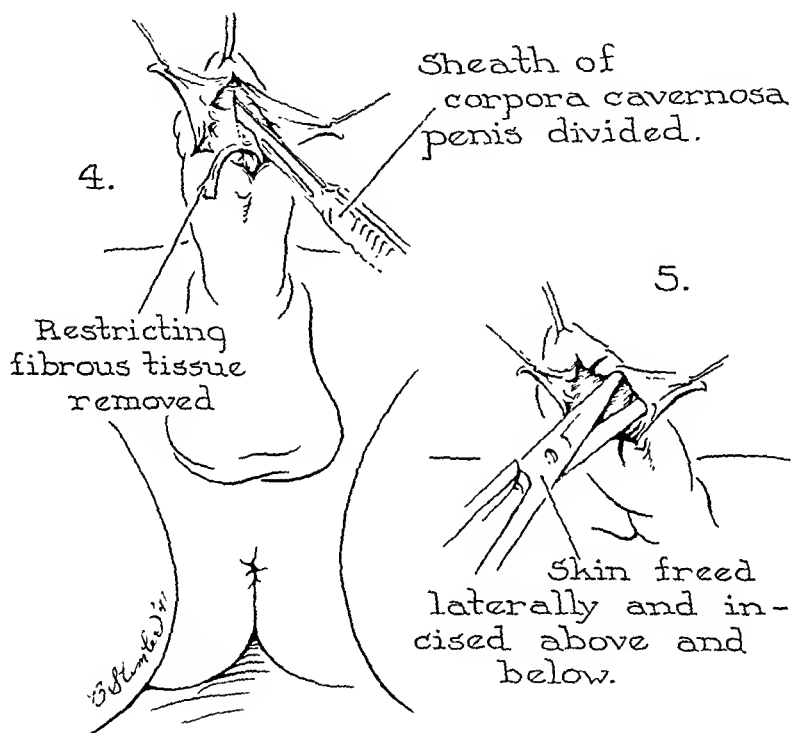
A. W. FARMER, M.D., TORONTO, CANADA

VARIOUS degrees of hypospadias, recognizable as glandular, penile, penoscrotal, scrotal, and perineoscrotal varieties are found.

In the first, treatment is not necessary. No serious disability is present. Meatotomy is performed occasionally for a pin-point opening. With the other types, besides the abnormal position of the meatus, there



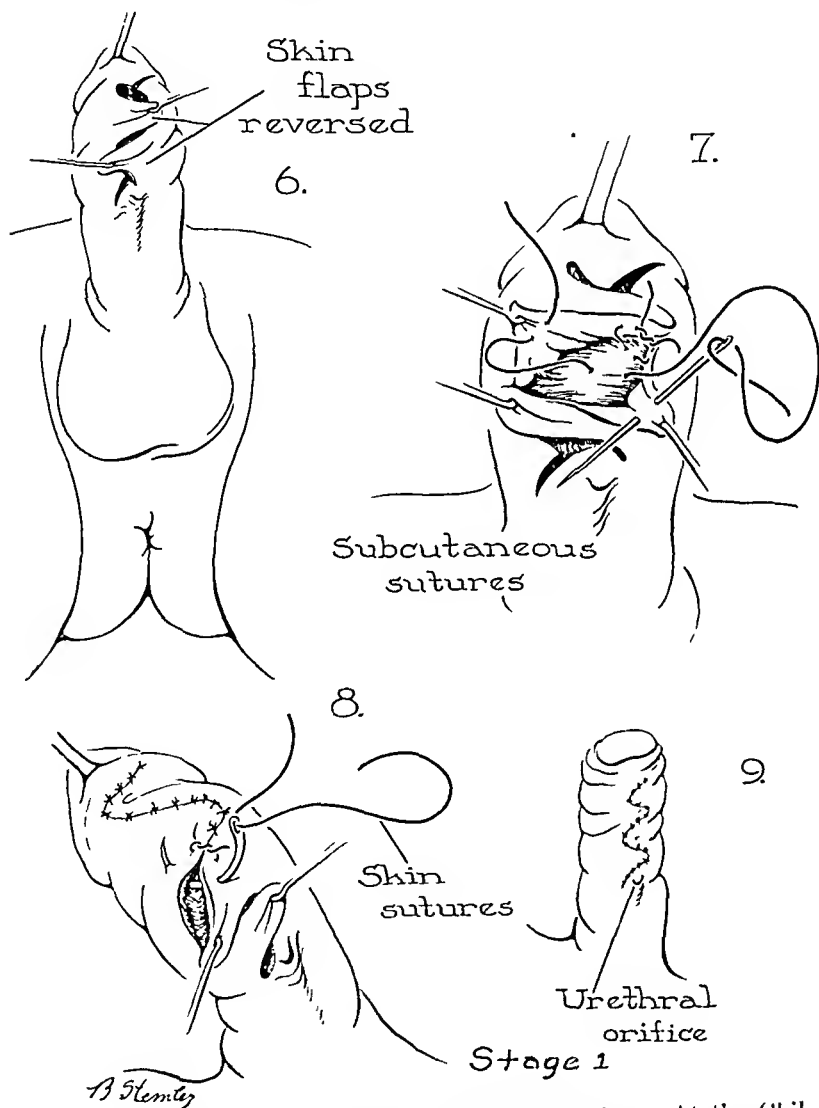
are accompanying deformities. The most constant is the presence of a tight shiny skin on the ventral aspect. Under this there is fibrous tissue where the corpus spongiosum is absent. A curvature results, frequently, varying in amount in direct proportion to the posterior displacement of the urethral opening. Other distortions may consist of an aplasia of the penis, a split scrotum, undescended testicles, and dyscrinism.



Stage 1

The treatment of these mild and severe varieties is the correction of the curvature and the manufacture of an urethra. The first procedure is performed as a complete operation in itself, of which the steps are shown in Figs. 1 to 9 in a diagrammatic manner. The incision is in the form of a Z-shaped plastic. Because of the limited distance between the glans and the urethral opening, the vertical limb of the Z may be very short. Dissection under the urethra frees it from surrounding tissues, and it is pushed posteriorly. Fibrous tissue on the ventral surface and from between the corpora cavernosa is removed. The skin is freed laterally on both sides. Further releasing incisions are often made, as shown in Fig. 5. All this allows the distal end of the penis to be extended, overcoming the curvature. Closure is obtained by subcutaneous,

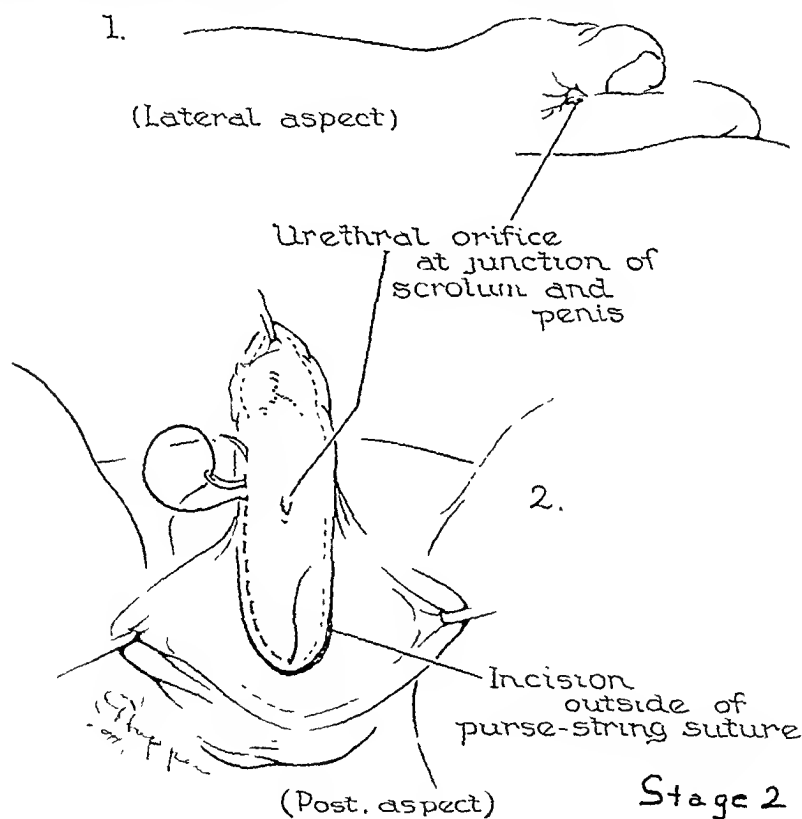
as well as skin, stitches. The former catch up the deep tissues, as represented in Fig. 7. The suture line is one of changing directions. The primary covering is important. The penis must be held straight until the skin wound is firmly healed. The incision is painted with varnish and dry gauze is wrapped around the organ. An elastic mesh, stitched to the skin at the base to prevent slipping, is sutured over the dressing, applying pressure. Collodion is smeared on, and hardens as a waterproof splint. It is left in place for fourteen days.



The second operation is designed to make an urethra. At the Children's Hospital in Toronto this had proved difficult. Ombredanne described a procedure which he claimed to be uniformly successful in

hundreds of cases. The steps to be described, and shown in Figs. 1 to 14 of the second stage, represent a considerable modification of his mode. I have operated upon about one hundred cases since 1932, occasionally making alterations, and the result is as shown.

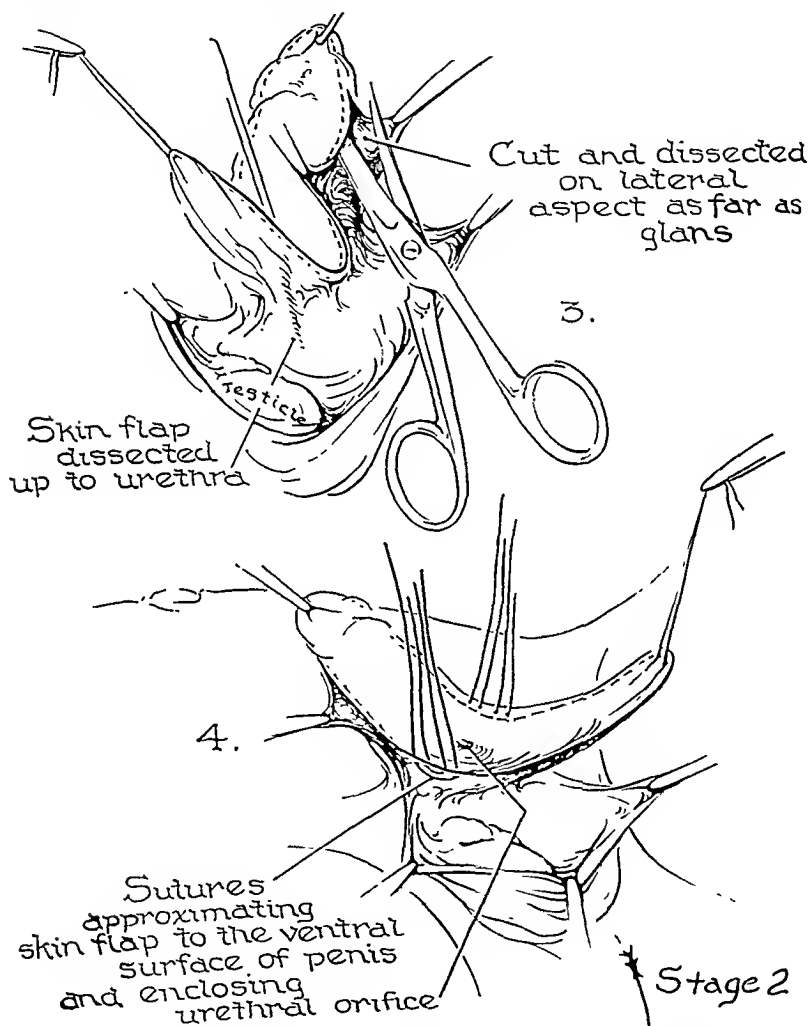
For diagrammatic purposes, the meatus has been placed at the penoserotol junction. A narrow flap is outlined so that the opening occupies a central position between the tip of the glans and the perineal end of the flap. It is uniform in width (about one-half inch) with tapering ends. A stainless steel wire suture is passed about the edges. After the initial incision, the raising of the flap is done largely with



scissors. Fig. 4 shows the application of sutures to form the urethra. Horsehair is preferred to silk. The stitches run from skin surface to skin surface, outside the wire thread. One edge is completed as far as the glans before the other is begun, sutures being tied as they are put in, left long, and thrown to the opposite side. When the glans is reached, the mucous membrane is cut, after tunneling beneath it with small, pointed scissors. With this method there is little bleeding. The membrane is stitched to the tip of the perineoserotol pedicle, the long

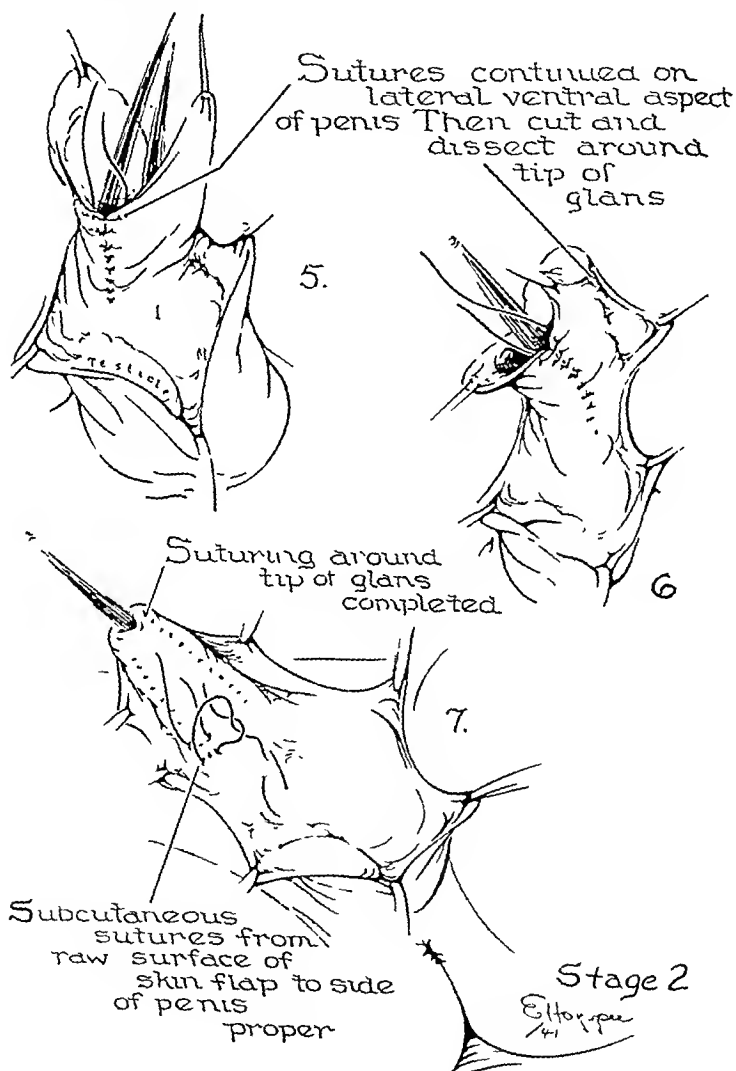
threads running from the new opening. The horsehair seam is reinforced by catgut.

Much raw area remains to be surfaced. Direct suture is satisfactory in the scrotal area, but rearrangement of the covering is necessary for the penis. The redundant foreskin is separated from the glans, and unfolded. A spotlight shining through it identifies any large vessels. The separation of the skin from the penis must be as far as its root. This

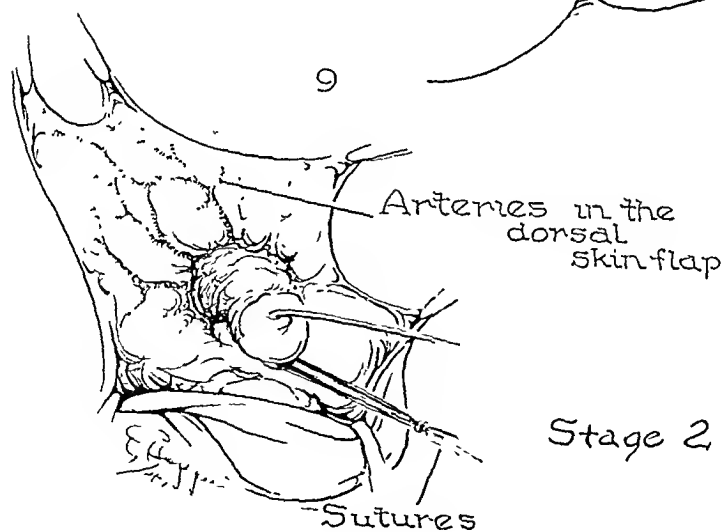
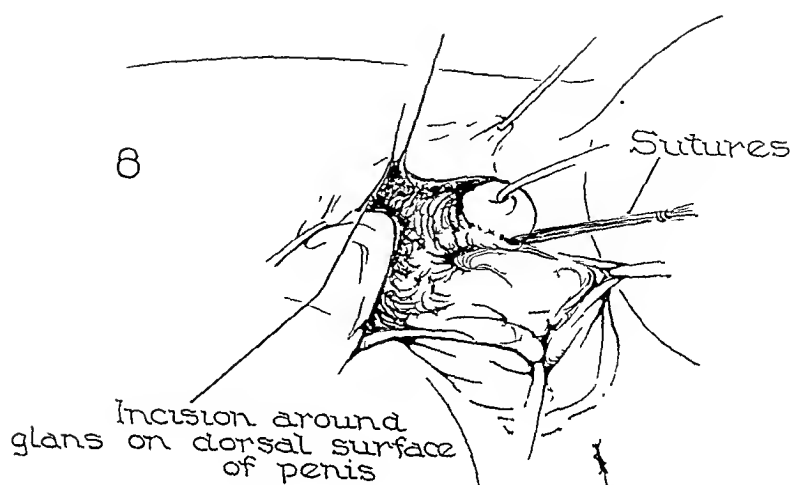


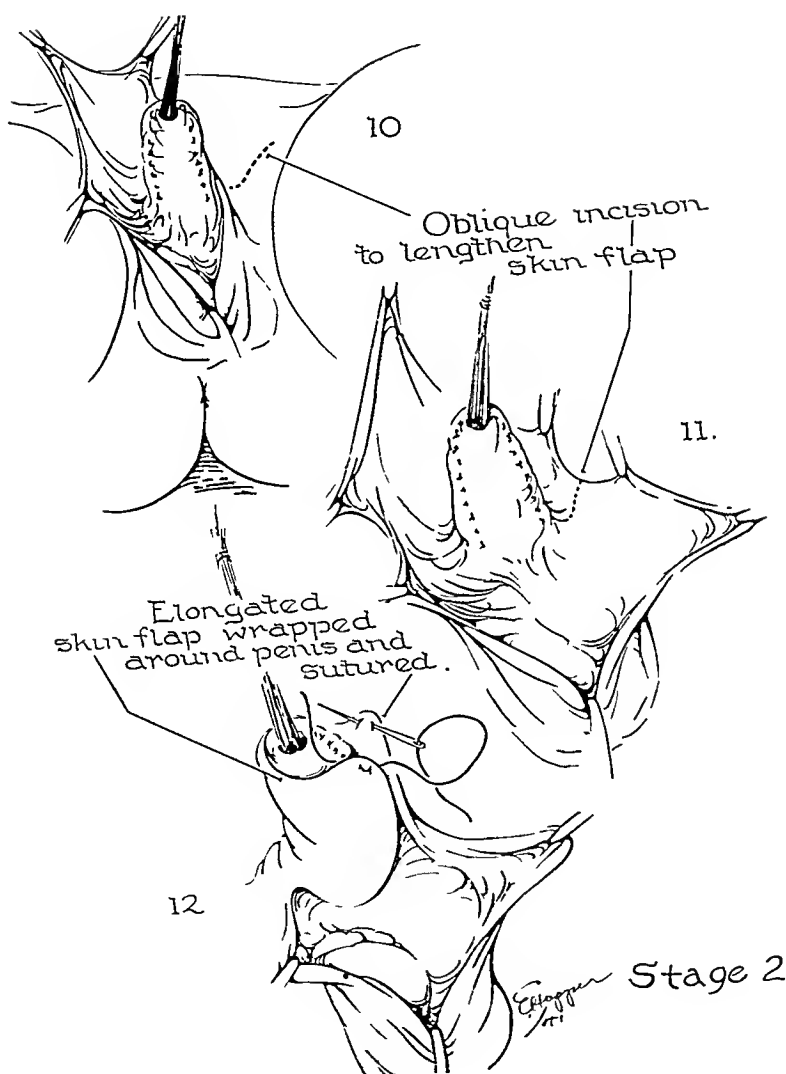
flap is then wound about the organ. Using transillumination, an oblique incision, as shown in Fig. 11, may be made to allow change in direction of the tissue without pulling too tightly along one margin. Subcutaneous as well as skin stitches are employed. The steel wire is tied with a little tension, and the ends left long.

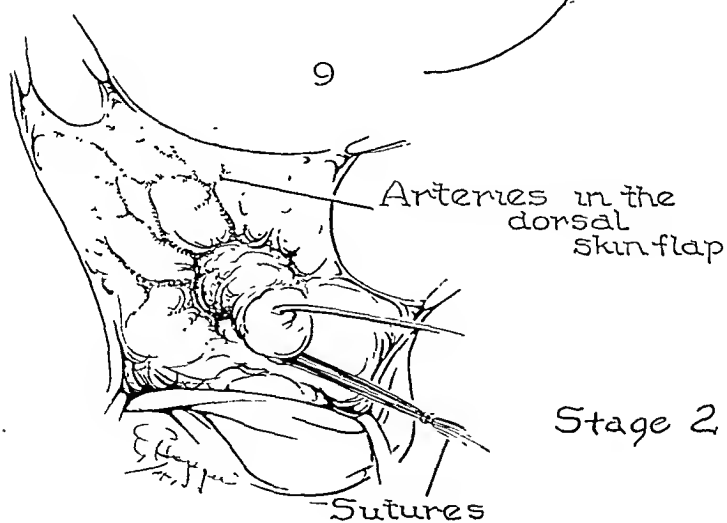
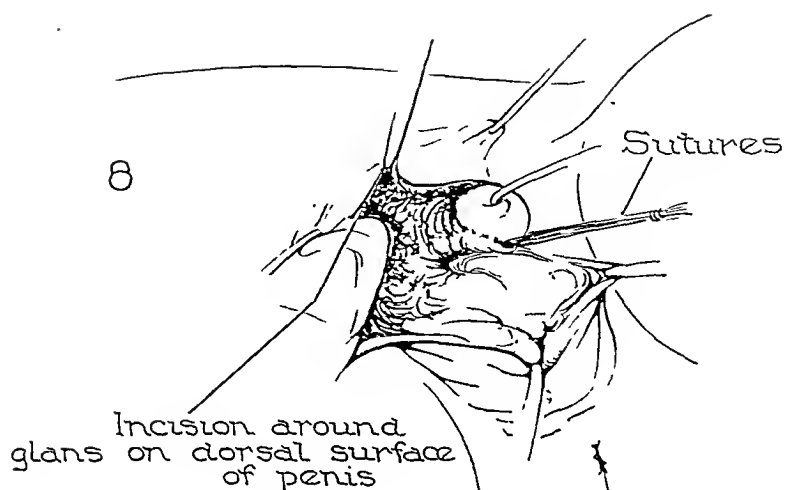
This operation takes about one and one-half hours to complete. The thin flaps must be handled carefully. Serotal varieties in children and adults are performed successfully in one stage. In such, the flap may be very long, its tip coming from near the anus.

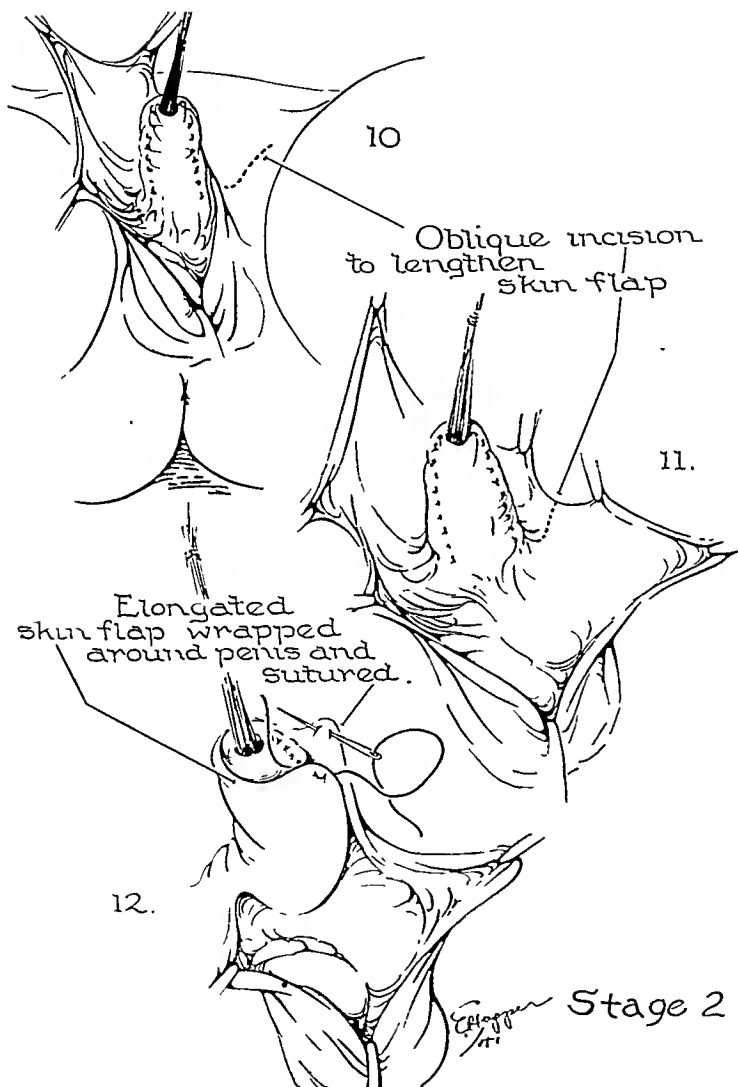


The postoperative care presents no difficulties. All patients have urinated voluntarily. Great edema of the tissues occurs, which subsides slowly so that a normal appearance is approximated in about ten to fourteen days. The penis, heavy with swelling, tends to flex at the penoserotal junction due to gravity. Support by gauze, as well as by fixing the long ends of the steel wire to the abdominal wall, is important,

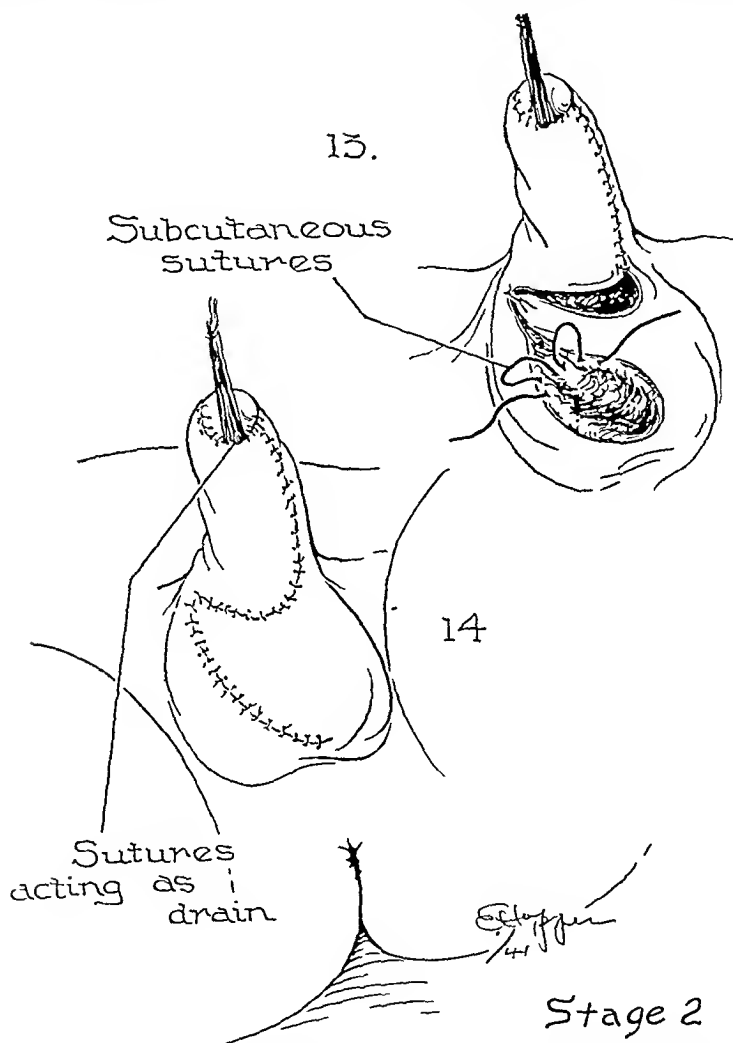








as the adjacent skin surfaces become macerated if left in contact. Routinely in recent times, patients have been placed on sulfathiazole.



In conclusion, approximately one hundred cases of hypospadias have been operated upon. The Ombrédanne method was not found to be completely satisfactory, particularly for severe types. It has been modified to give a better cosmetic and functional product more quickly. The results have been uniformly good. No sidetracking of urine is necessary, and hospitalization is short.

SUBDURAL AIR

PRELIMINARY REPORT OF ITS USE AS A METHOD OF PREVENTING POSTOPERATIVE CORTICOMENINGEAL ADHESIONS

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CONVULSIONS which follow otherwise successful cerebral operations are, unfortunately, all too common. They were frequent enough in the experience of Cushing following the excision of meningiomas of the hemisphere to warrant the administration of phenobarbital as a routine measure in an attempt to prevent the establishment of an epileptic pattern. In the opinion of many neurosurgeons the incidence of convulsions following the drainage or excision of a cerebral abscess is 50 per cent or more, and following compound depressed fractures of the skull is between 5 and 20 per cent.

If convulsions arise after total excision of a cerebral tumor, successful drainage of a brain abscess, or complete débridement of a compound depressed skull fracture, it is logical to assume that they are due to the resulting brain scar. Credence is lent to this view by the fact that in the hands of Penfield, Foerster, and others excision of corticomeningeal cicatrices has been followed by cessation or amelioration of the epileptiform seizures in a goodly proportion of cases.

Penfield and Buckley¹ have shown in dogs that the amount of intracerebral scar varies directly with the amount of injured cerebral tissue which "has been left behind." The same principle has been shown by Penfield² to apply to cerebromeningeal adhesions. It is for this reason that in compound fractures of the skull the accepted neurosurgical procedure is to remove all damaged brain substance until healthy brain tissue has been encountered.

In spite of the most careful technique, however, a denuded and traumatized brain surface invariably follows any transcortical procedure. When this surface comes in contact with the overlying dura, scalp, or bone, adhesions are bound to result. In order to prevent this contact until healing is in progress we suggest the use of subdural air. It is hoped that this method may prove of value in preventing convulsive attacks following war wounds.

The following four case histories illustrate the development of the technique of this method up to the present time.

CASE 1—L. O'T, a white female child, aged 2½ years, entered the University Hospital April 30, 1937, because of convulsions. History revealed that at the age of twenty months the patient developed weakness of the left leg which gave rise

¹First report was presented at the Second Annual Meeting of the Central Surgical Association, Chicago, Ill. Feb. 27 and 28, 1942. Complete report presented to the Harvey Cushing Society, New York, N. Y., May 20, 1942.

to the diagnosis of a left spastic monoplegia. Six weeks prior to admission, there was noted increasing weakness of the left leg, abnormal salivation, persistent vomiting of a nonprojectile type, and frequent convulsions, especially while asleep, characterized by grinding of the teeth, "stiffening out," and rolling of the eyeballs. During an attack witnessed in the hospital, there was twitching of the face and extremities for forty-five seconds, with unconsciousness. Significant findings were abnormal drooling of saliva, spastic weakness of the left leg, and extensor plantar response on the left. Funduscopic examination was negative. Pneumo-encephalogram (Fig. 1) revealed evidence of a space-occupying lesion deep in the right temporal lobe. At operation an encapsulated tumor, approximately the size of a golf ball, was encountered by a transectorial incision through the mid-temporal region 2 cm. in depth. The entire tumor was removed. The ventricle was not entered. The dura was completely closed and the bone flap replaced. Pathologic diagnosis was cavernous hemangioma.

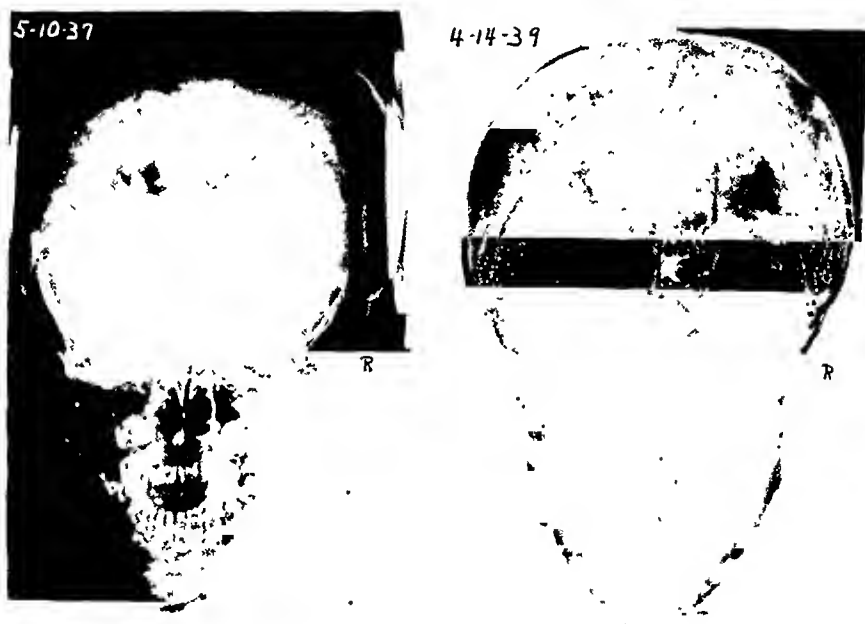


Fig. 1 (Case 1).—A, 5/10/37, pneumo-encephalogram demonstrating deep-seated right temporal lobe tumor. B, 4/14/39, pneumo-encephalogram demonstrating absence of tumor and dilatation of right ventricle with traction to side of area of cortico-meningeal adhesions.

Postoperatively the patient showed a marked weakness of the left arm and leg which gradually improved. She was discharged on the sixteenth postoperative day with a mild left hemiparesis.

A year and one-half later the child developed left-sided jacksonian attacks. Pneumo-encephalogram (Fig. 1) revealed a generalized increase in size of the right lateral ventricle. Subarachnoid channels in the region of the operative site showed no drainage, with no evidence of recurrence of the tumor. The patient was discharged on phenobarbital, $\frac{1}{2}$ gr., three times a day.

She returned about two weeks later because of increasing severity of left-sided jacksonian attacks. Another pneumo-encephalogram was performed which was identical with the preceding one.

The focal epilepsy continued in spite of medication with phenobarbital and, consequently, the patient was readmitted to hospital for reoperation Sept. 17, 1941, approximately four years after the original removal of the tumor. It was felt that the persistent jacksonian attacks were due to a corticomeningeal cicatrix at the operative site. Consequently, operation was performed through the old scalp incision, the bone flap was re-elevated with no damage to the underlying dura, and it was found that the cortex was firmly adherent to the dura over an area four by five inches in diameter. The adhesions were extremely vascular and were completely freed from the overlying dura. Beneath the dura the previous cortical incision could be made out clearly. The convolutions around it were quite normal except for the adhesions. At this point in the operation the wish was expressed that re-formation of these adhesions could be prevented. It was suggested that an attempt be made to keep the cortex away from the dura by the instillation of subdural air. Consequently a soft rubber catheter with holes cut in the wall and surrounded by metaphen in oil pack was placed over the operative site and brought out through

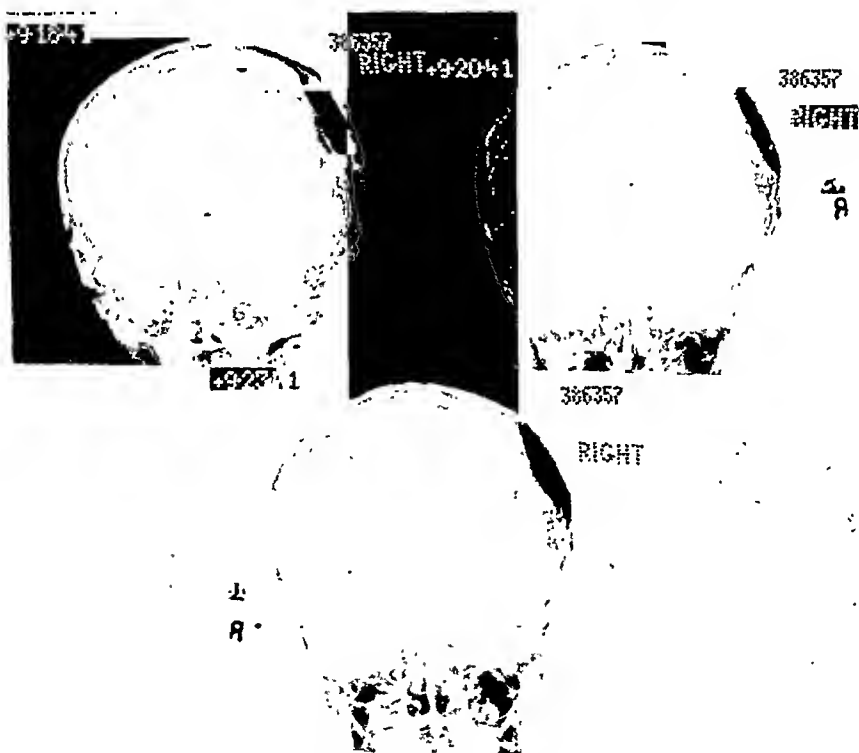


Fig. 2 (Case 1).—Subdural aerograms after excision of corticomeningeal adhesions showing brain held away from the overlying dura and bone; rate of air absorption may be noted.

a small stab wound in the middle of the flap. The dura and scalp were closed with silk in the usual manner. The following day lumbar puncture was performed and 30 c.c. of bloody fluid drained. During this procedure it was ascertained that air was being drawn into the rubber catheter by placing drops of sterile saline solution in the mouth of the catheter and watching them disappear down the tube. The catheter and pack were then removed and the patient taken immediately to the x-ray room. Stereoscopic views (Fig. 2) revealed

an adequate amount of subdural air over the operative site to depress the entire right hemisphere away from the dura. Following this the patient was kept in a semi-upright position and seemed little affected by the procedure. Subsequent x-ray examination revealed gradual absorption of the subdural air and four days later the procedure was repeated after placing a needle through the scalp at the site of an old trephine opening. Again it was ascertained that air was entering the subdural space on lumbar puncture. This was confirmed by x-ray examination which again showed the cortex well away from the dura with no evidence of adhesions. Subsequent x-rays revealed gradual absorption of the subdural air over a period of four days. Again no untoward reaction from the procedure was noted.

It has been eight months since operation and the mother states that there has been no recurrence of the attacks in any form and that the child is attending school regularly. She has had no anticonvulsant medication since discharge.



FIG. 3 (Case 2).—A, subdural aerograms following excision of corticomeningeal adhesions. Silver clips were placed at the time of operation to mark operative site which is shown here to be held well away from contact with the overlying dura. B, 11/11/41, shows result of subdural refill done four days postoperatively.

CASE 2.—M. E., a 10-year-old white male, entered the University Hospital Oct. 21, 1941, because of convulsive seizures. At the age of 11½ years a débridement had been performed for a compound depressed fracture in the right frontal region. Generalized convulsions were first noted seven years later, gradually increasing in severity in spite of anticonvulsant medication until they occurred three to four times a week. Examination was completely negative except for an old scar over the right frontal region beneath which could be palpated a small operative defect in the skull. This defect was confirmed by x-ray. Localizing electro-encephalogram revealed diffuse disturbance in brain function with slowing of wave pattern and signs of irritability. There was additional evidence of cortical brain damage, more marked in the right posterior frontal region, spreading to the anterior frontal and parietal regions. Pneumo-encephalogram was reported as negative. A diagnosis was made of post-traumatic epilepsy due to a corticomeningeal scar in the right frontal region. Consequently, on Nov. 6, 1941, a small four-holed osteoplastic flap was turned down, centering about the bony defect. The dura was incised and directly beneath the site of the penny-sized bony defect there was found an area in which the pia-arachnoid was firmly adherent to the overlying dura. Two large vessels were seen coursing through this adhesion into the cortex. These were coagulated

and severed, allowing the cortex, which appeared otherwise normal, to fall away freely. An attempt to explore the cortex in all directions was made but this was difficult. Consequently, a lumbar puncture was performed and 22 cc of clear and colorless spinal fluid were removed. It was found that following this the brain had fallen away sufficiently to allow complete exploration of the cortical surface of the frontal lobe. No further abnormality was seen. The dura was closed tightly about a small soft rubber catheter which was brought out through one of the trephine openings after the bone flap had been replaced. Repair of the bony defect was effected with a small osteoperiosteal graft. The skin flap was closed in the customary fashion about the rubber catheter. The patient was placed in a sitting position and an additional 15 cc. of spinal fluid were removed by lumbar puncture. It was ascertained, by disappearance of drops of saline solution in the catheter mouth, that air was entering the catheter. The catheter was then removed. Immediate x-ray examination (Figs 3 and 4) revealed air in the right subdural

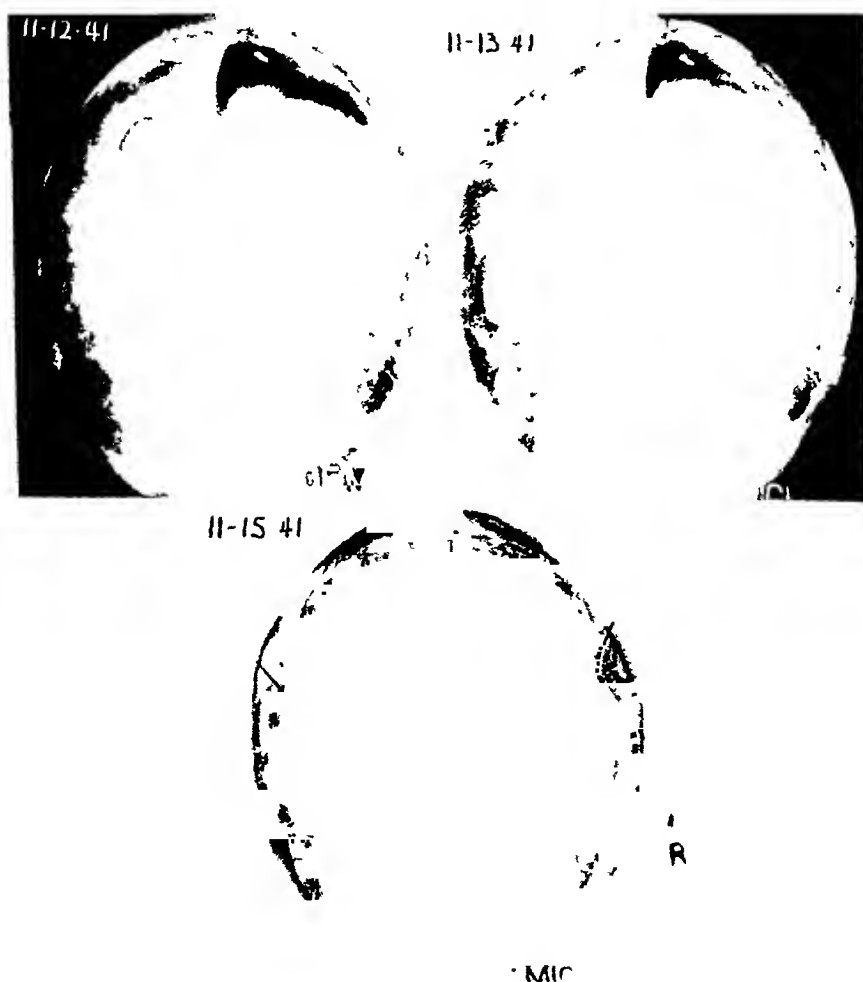


Fig. 4 (Case 2) —Subdural roentgenograms following excision of corticomeningeal adhesions showing rate of absorption of air after subdural refill four days postoperatively.

space and evidence that the cortex was well away from the overlying dura. Following operation the patient complained of headache, of no particular severity. Five days later a small lumbar puncture needle was placed through the scalp into one of the trephine openings. Lumbar puncture was performed in the sitting position and 60 c.c. of clear and colorless spinal fluid removed. It was ascertained that during this drainage air was sucked in freely through the scalp needle. Again x-ray examination revealed good subdural filling with the cortex away from the dura. Checkup x-rays revealed that this subdural air was still present, although in diminished quantity, two days later. The patient has had no recurrence of his convulsions to date, 7 months postoperatively.

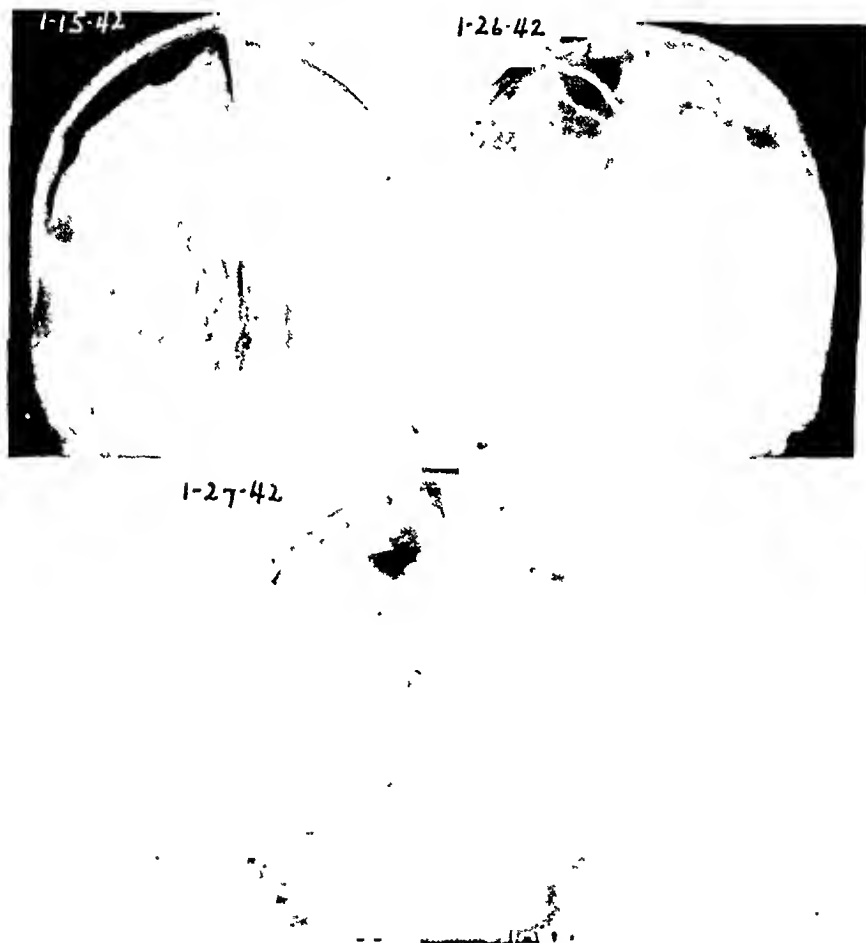


Fig. 5 (Case 3).—Subdural aerograms A, 1/15/42, preoperative, suggesting cortico-meningeal adhesions at tip of right frontal lobe, old bony defect over right frontal sinus reveals site of previous drainage of brain abscess. B, 1/26/42, immediately postoperative, shows small osteoplastic bone flap with catheter in subdural space. C, 1/27/42, second postoperative day, reveals good subdural filling over right frontal pole, adhesions now absent.

CASE 3.—R. M., a 20 year old white male, entered the University Hospital Jan. 13, 1942, with a typical story of petit mal epilepsy of six months' duration. Past

history revealed that the patient had suffered a compound fracture through the right frontal sinus followed by a brain abscess. This was successfully drained elsewhere. The "spells" of which he was unaware were stated to consist of throwing the head back and forth, staring straight ahead for a few seconds, and then returning to normal without sequelae. The attacks were of increasing frequency and because of them the patient was unable to obtain employment. Examination was negative except for a small pulsating defect lying beneath a scar over the medial portion of what had been the right frontal sinus. X-ray revealed a small bony defect in this region. Electroencephalogram suggested a grand mal type of convulsive disorder as well as some evidence of damage in the right frontal pole. Pneumoencephalogram demonstrated slight dilatation and forward projection of



Fig. 6 (Case 3) —Postoperative refill subdural aerograms showing absence of previous adhesions, maintenance of subdural space over operative site, and rate of air absorption.

the frontal horn of the right lateral ventricle. On Jan. 15, 1942, a trephine opening was made in the right parietal region and the dura was opened. A lumbar puncture was performed with the patient in a sitting position and 10 c.c. of spinal fluid were removed at which time it was observed that the cortex beneath the

trephine fell away for the distance of approximately 1 cm. The scalp incision was closed and the patient was immediately taken to the x-ray room where stereoscopic films (Figs. 5 and 6) revealed evidence of corticomeningeal adhesions in the region of the previously described bony defect. On Jan. 26, 1942, a small right frontal osteoplastic flap was turned, its base along the supra-orbital ridge and its medial border along the midline. It was found that the dura and the underlying brain were firmly adherent to the bony defect in the region where the frontal sinus had been. First the dura, then the adherent brain were freed. Following this the scarred cortex of the tip of the frontal pole, measuring approximately 3 cm. in diameter, was completely excised into healthy brain tissue, including a small cyst filled with clear and colorless fluid. Exploration revealed no further abnormality. A soft rubber catheter was placed in the defect, the dura was closed, and the catheter brought out through one of the trephine openings. The bone flap was replaced and the scalp closed in the usual fashion about the catheter. Next the patient was placed in an upright position and 60 c.c. of spinal fluid were removed by lumbar puncture. Air in the subdural space was demonstrated by x-ray (Figs. 5 and 6). Subdural air refills were done on the fourth and seventh postoperative days (Fig. 6). The cortical defect was demonstrated to lie well away from the overlying dura on these occasions and on checkup examinations. Postoperatively the patient was alleged to have had one petit mal attack and he was discharged on the fourteenth postoperative day. A checkup report five months after operation states that he has had only one other questionable attack.



Fig. 7 (Case 4).—Subdural aerograms. A, 1/29/42, reveals failure to fill subdural space in right frontal region due to extensive corticomeningeal adhesions. Bony defect from previous drainage of brain abscess may be seen overlying the silver clips. B, 2/11/42, reveals brain well away from overlying bone and dura following excision of brain scar and adhesions and subsequent subdural air instillation.

CASE 4.—J. A., a 26-year-old white male, entered the University Hospital Jan. 23, 1942, in a postepileptic stupor. Six years previously at this hospital a bilateral Killian operation and drainage of an encapsulated left frontal abscess had been performed.

The patient had been perfectly well until the Fall of 1941, when he had a convulsion, following which he became disoriented and irrational for a day. Following a second attack two days before admission he remained semistuporose and did not become clear until three days after admission.

Examination at this time was entirely negative except for a transverse scar at the hairline beneath which a pulsating defect about one and one-half inches in

diameter was seen. Roentgenograms revealed a postoperative defect along the left supra-orbital ridge and a circular defect in the left frontal region.

On Feb. 2, 1942, a trephine opening was made in the left parietal area and the dura opened. A lumbar puncture was performed with the patient in the sitting position and 125 c.c. of spinal fluid were obtained. The brain was seen through the trephine opening to have fallen away from the dura for a distance of almost 2 cm. X ray examination (Fig. 7) showed evidence of a large amount of subdural air with extensive adhesions surrounding the bony defect in the region of the left frontal pole. The patient was in no way upset by this procedure.

Operation was performed four days later, at which time the extensive adhesions were divided and the scarred frontal pole was excised. The anterior horn of the ventricle was opened during the procedure. The entire frontal lobe now lay free from the overlying dura. An osteopariosteal graft was placed over the bony defect. Just before closure of the scalp, lumbar puncture was performed and approximately 100 c.c. of spinal fluid were removed. The scalp was closed in the usual manner. X rays (Fig. 7) revealed the air in the subdural space and evidence that the frontal lobe lay free from the overlying skull in all directions. The injection of subdural air was repeated four days later after inserting a needle through the scalp and again five days later after a trephine opening had been made in the left posterior parietal region. There was no evidence by x ray that adhesions had reformed. The patient was discharged on the fourteenth postoperative day, on phenobarbital, $\frac{1}{2}$ gr., three times a day. A report received four months after operation states that he has been free of attacks and is working full time.

DISCUSSION

The four cases described above all suffered from a convulsive disorder following an otherwise successful eradication of a cerebral lesion. It seems logical to assume that the corticomeningeal scars and adhesions resulting from the original operative trauma were contributing causes of the convulsions. In an attempt to eradicate these epileptogenic foci they were excised surgically. To prevent the subsequent re-formation of adhesions between the brain and the overlying dura, bone, or scalp, subdural air was instilled on several occasions postoperatively. X-ray examination revealed that the subdural air was effective in accomplishing this purpose over a limited period of time. It is still too early in the postoperative period to be able to state definitely the extent to which this procedure will have minimized adhesion formation or modified the convulsive disorder. One case, however, (Case 1), has been free of jacksonian attacks for eight months in spite of a well-established pattern preoperatively. It is hoped to recall these patients for re-examination with subdural air studies, thus proving or disproving the re-formation of corticomeningeal adhesions.

We realize fully that the use of subdural air cannot prevent brain scar formation which may, in itself, act as an epileptogenic focus. It is felt, however, that prevention of contracting adhesions between the brain and its overlying coverings would eliminate abnormal traction effects and vascularization, both of which have been emphasized as important factors in the production of convulsive phenomena.

The use of subdural air postoperatively to prevent the formation of corticomeningeal cicatrices is still too new and untried a procedure to warrant any definite statements. However, certain points concerning it can be pointed out at this time.

1. It can be used without ill effects upon the patients. In all of the above cases it was accompanied only by a certain amount of headache. This headache, however, was much less severe than that found associated with pneumo-encephalogram.

2. The removal of moderate amounts of spinal fluid (up to 125 c.c.) results in an adequate amount of air being drawn into an open subdural space to visualize localized areas of this space satisfactorily by x-ray. It can also be used to visualize corticomeningeal adhesions, as has been pointed out in the past by Penfield and Noreross,³ Hemmingson,⁴ and Olivecrona.⁵

3. It has been possible to separate, and maintain separated, the operative field from the overlying dura, bone, or scalp by subsequent refills of subdural air, over as long a period as we have desired.

4. The technique is simple and not dangerous to the patient. Our experience to date suggests the following procedure to be most efficacious: When a corticomeningeal cicatrix is suspected a trephine is made well away from the probable site of the lesion but on the same side. The dura is opened and up to 125 c.c. of spinal fluid are drained by lumbar puncture in the sitting position. The site of the lesion is kept uppermost and the scalp incision is closed. In this way air collects about the cicatrix. Tangential x-rays are taken from several directions. Following excision of a corticomeningeal cicatrix (or, for that matter, any transectorial procedure which might produce postoperative adhesions), the patient is placed in an upright position with the subdural space open (either directly or by means of an indwelling catheter) and lumbar drainage performed. If the patient's condition warrants it, x-rays may be taken at this time or within the next twenty-four hours. The absorption of the subdural air may be followed by x-ray studies. In our experience air in the subdural space becomes absorbed in four or five days. Refills may be done either by reopening the trephine, inserting a lumbar puncture needle through the scalp overlying a previous trephine, or, if necessary, making a new trephine opening. The site of the lesion should be kept uppermost.

We have much to learn concerning this new procedure. Some of the factors which remain to be clarified are: (1) The length of time necessary to refill the subdural space in order to prevent the formation of adhesions between an operative field and the overlying dura, bone, or scalp; (2) whether the method can be used effectively following original operation such as excision of a meningioma or débridement of a compound skull fracture; (3) the details of x-ray technique for exact visuali-

zation of a particular area either for the purpose of demonstrating corticomeningeal adhesions or their absence before and after operation.

Past experience has thrown a certain amount of light on these factors. For example, in a case of brain abscess which had been drained twenty-one days previously, through an inch and one-half frontal bone defect, the removal of 74 c.c. of spinal fluid by lumbar puncture unexpectedly resulted in retraction of the firmly adherent frontal lobe to a depth of approximately 2 cm. beneath the skull. No untoward effects were noted. The conclusion reached from this observation is that extensively organized corticomeningeal adhesions can be broken down even after the elapse of three weeks' time. It has been observed in two cases of the above series that subdural air has prevented the formation of adhesions for at least ten days. There is no reason to suppose that adhesions could not be prevented indefinitely by subsequent refills of subdural air were it feasible technically or actually necessary. In one case (Case 4) in which the ventricle was opened, the subdural air seemed to be more rapidly absorbed. In regard to x-ray technique it was found that best visualization of the operative site was obtained when the head was placed so that the defect was uppermost and when tangential stereoscopic views were obtained.

SUMMARY

A new and simple method for the prevention of postoperative corticomeningeal adhesions is described, suggesting the use of subdural air instillations. It is hoped that by the prevention of such adhesions the frequency of convulsions following otherwise successful cerebral operations may be lessened.

REFERENCES

1. Penfield, W., and Buckley, R. C.: Punctures of Brain; Factors Concerned in Gliosis and in Cicatricial Contraction, *Arch. Neurol. & Psychiat.* 20: 1-13, 1928.
2. Penfield, W.: The Mechanism of Cicatricial Contraction in the Brain, *Brain* 50: 499, 1927.
3. Penfield, W., and Norcross, N. C.: Subdural Traction and Post-Traumatic Headache; Study of Pathology and Therapeutics, *Arch. Neurol. & Psychiat.* 36: 75-95, 1936.
4. Hemmingson, H.: Roentgenologic Investigations on the Extracranial Subdural Space With a View to Revealing the Presence of Subdural Adhesions, *Acta radiol.* 21: 375-391, 1940.
5. Olivecrona, H.: Cortico-Meningeal Sears in Traumatic Epilepsy; Localization by Pneumographie Examination of the Subdural Space, *Arch. Neurol. & Psychiat.* 45: 666-671, 1941.

A METHOD OF EXTENSIVE LAMINECTOMY WITH REPLACEMENT OF REMOVED LAMINAE

ALBERT S. CRAWFORD, M.D., DETROIT, MICH.

(From the Division of Neurological Surgery of the Henry Ford Hospital)

SURGERY is being more and more successfully used for the relief of pain in a large group of cases with the diagnosis of sciatic neuritis. Laminectomy, with varying degrees of bone removal, has seemed to give the best results in cases where there has been impingement upon one or more nerves by ruptured intervertebral discs, thickened ligamenta flava, and the other anatomic structures which surround the nerves as they pass through the intervertebral foramina.

The easily approachable, sharply localized protruding masses from ruptured intervertebral discs can often be adequately removed with minimal or no bone removal. This has the advantage of prompt convalescence and little or no weakening of the back.

But in our experience there are some cases with good clinical history and findings of ruptured discs which at operation have shown neither a ruptured disc nor a thickened ligamentum flavum, but where the cause of nerve impingement has been one or more of the following anatomic structures: (1) The upper lip of the fifth lumbar facet, with a relaxed joint, associated with increased lumbosacral lordosis; (2) Hypertrophic arthritis resulting in a flaring out of the borders of the vertebral bodies, thus simulating a prominent intervertebral disc; (3) A structurally small intervertebral foramen due to bony changes or to increased tissue, including dilated lumbar veins, surrounding the nerves in the foramina.

Clinically these cases are similar to those due to ruptured discs, but are less likely to have clear-cut traumatic histories, usually have a more prolonged and intermittent course, and although they may have improved with conservative therapy, have had repeated recurrences of pain and finally have become incapacitated. They may have bilateral signs or symptoms which may involve either or both of the fourth and fifth lumbar nerves.

To adequately expose these nerves on both sides by the usual method of laminectomy with rongeurs may leave a structurally weak back, as the facets may have to be removed. To correct this, a bone graft from the tibia has been the method usually employed. This means a prolonging of the period of convalescence.

In attempting to meet this latter problem, lately we have been removing in one piece, with chisel and mallet, the entire dorsal arch composed of a spine, lamina, and attached facets (Figs. 1, 2, and 3).

An excellent exposure of both nerves throughout their entire course through the foramina is given in Fig. 4. In this photograph, the area between 1, 2, and 3 is one where a somewhat thickened ligament may compress the nerve, 2, against a prominent disk margin, 4. This area is

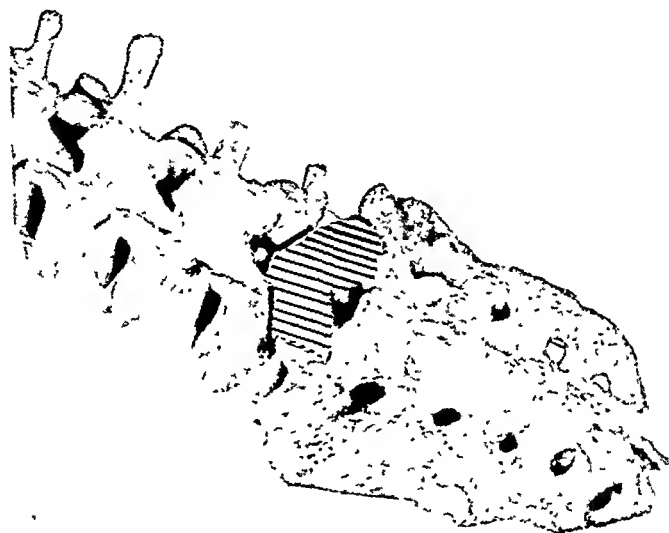


Fig. 1.—Photograph of lumbar spine and sacrum. The part which is crosshatched is the piece removed with a chisel.

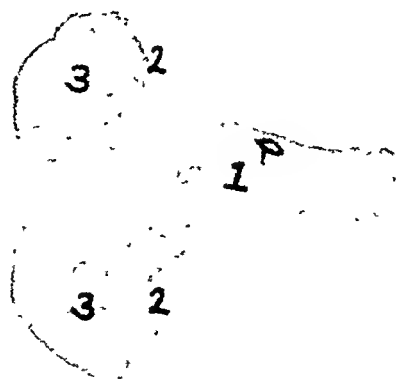


Fig. 2.—Dorsal view of the removed dorsal arch of the fifth lumbar vertebra, 1 is the spine, 2 the place where the arch is cut through with a chisel, 3 the dorsal part

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off to insure bony ankylosis, the piece is then returned to its bed and sutured in place with silver or stainless steel wire between the adjacent spines and facets. The patient is kept on a Bradford frame for a few days and then has a back brace fitted to be worn until the graft is safely grown in place.



Fig. 5—Left lateral view of lower three vertebral bodies and sacrum. X shows slight lipping of the lower margin of the fifth lumbar body. This, if more extensive, can encroach on the lumen of the intervertebral foramen.

We have done this type of operation on seven patients during the last ten months. Thus far it has proved to be satisfactory in giving excellent exposure for thorough decompression without the resultant weak backs which almost certainly would have resulted by the old method. Also, the patients have been able to return to active work sooner than they would have with tibial bone grafts.

This is, of course, only a small group of cases to serve as a reliable guide, and more time should pass to see if there might develop any unfavorable after-effects. We believe this method is worthy of further trial in cases where thorough exploration is indicated bilaterally. We do not advocate its use where the lesion is certainly unilateral and where it can be adequately relieved with a hemilaminectomy.

also shown in Fig 5. Sometimes we have had to chisel off the overhanging edge of the facet (5, Fig. 4), to free up an adherent involved nerve. At times, enlarged veins, accompanying the nerve through the foramina, appear to be an important etiologic factor.



Fig 3—Ventral view of the removed dorsal arch. 1 is the portion of the dorsal arch cut through with a chisel. 2 is the ligamentum flavum. 3 articular surface of the facets.

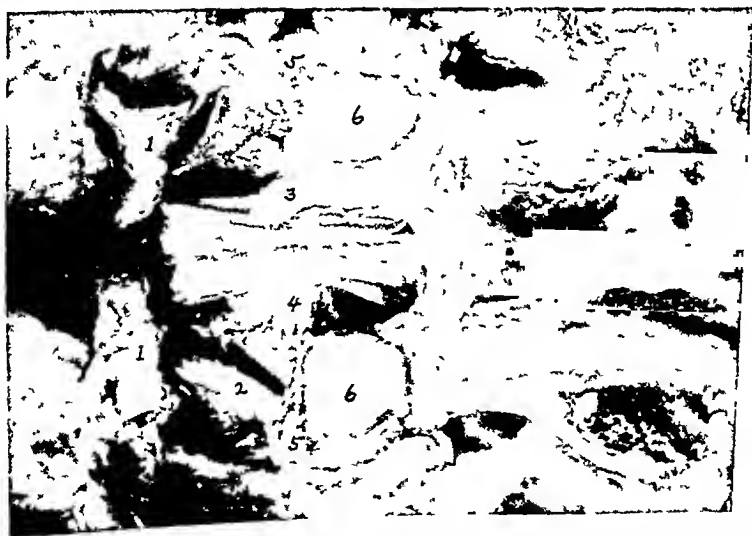


Fig 4—Dissection specimen on cadaver showing the area exposed by removal of the dorsal arch (Figs 1, 2, and 3 above). 1 is the place cut through with a chisel. 2 the nerve freed up of surrounding tissues. 3 ligamentum flavum. 4 underlying intervertebral disk. 5 overhanging margin of the facet. 6 cartilaginous upper surface of the facet.

After the nerves have thus been adequately decompressed and the removed bone fragment trimmed up so it cannot itself later cause nerve impingement, and the cartilage of the facets (6, Fig. 4), has been scraped

little hope of appearing upon the programs of the surgical sections of the American Medical Association with any regularity since the number of papers accepted is small and many of the places on the programs are assigned to senior surgeons whose reputations are established. In the past, similar problems have been experienced in the case of the meetings of the American College of Surgeons. Moreover, due to the very limited number of members, election to membership in the senior surgical societies is almost out of the question for men at the age of thirty or thirty-five. Therefore, a surgeon is apt to approach middle age before he is considered for membership in one of these older societies.

The conditions just enumerated have conspired to bring about the unfortunate situation wherein these promising young men in surgery have received too little encouragement to continue with original investigative work after completion of their training, especially at the time when stimulation and inspiration are needed most. Since relatively few of the men who complete a surgical residency will embark upon an academic career, it is apparent that the majority of them will leave a busy surgical clinic, often in a teaching center, to enter consultation practice. This abrupt transition from an environment where research and investigation are fostered and encouraged, to the routine duties of private practice is only too apt to result in a cessation of productivity resulting in a number of barren years which, under more favorable circumstances, might be made most profitable. That this problem is not especially new and that it has been fully appreciated by other groups, is manifested in the important and successful innovation inaugurated last year by the American College of Surgeons in its Forum on Fundamental Surgical Problems. Likewise, the Society of University Surgeons, although somewhat more restricted in its scope, was organized for a similar purpose.

The details of the organization of the Central Surgical Association having been completed by the Founders' Group and Founder Members, the society has been seen off to a good start and the active management of its affairs can soon be taken over by the junior members. While the consummation of these original plans has been considerably interrupted by the war, it is to be hoped that in the near future all of the activities of the organization will be in the hands of those for whom it was founded.

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Editorial

The Central Surgical Association

THE second annual meeting of the Central Surgical Association was held in Chicago, Feb. 27 and 28, 1942. Many of the papers presented at that meeting are published in this issue of SURGERY. The society was founded in the Spring of 1940 by a group of surgeons representing the Midwest, who first met at the invitation of Dr. Roy D. McClure for the purpose of discussing the possibilities of such a society. In general, the reaction to Dr. McClure's suggestion was favorable.

When a new surgical society is founded, obviously, if it is to survive, there must be evidence of a sufficient need and a place for it. In this particular instance the aims were twofold, the first being largely the need from a geographic standpoint. For many years certain sections of the country had been represented by their regional surgical societies concerned with the more purely scientific aspects of the practice of surgery. Thus, there were already in existence the Southern Surgical Association, the Western Surgical Association, the Pacific Coast Surgical Association, the New England Surgical Society, and a number of others. The great Middle West, although containing a number of important medical centers, had been singularly devoid of a comparable society recruiting its members, for the most part, from the Central States and Canada and holding meetings in cities of medical interest in the Midwest. It seemed no more than reasonable that this section of the country should have its own organization and one whose prestige would be equal to that of the afore-mentioned societies.

The second purpose of the proposed organization seemed even more important to those responsible for its establishment. In this respect the society was planned ultimately to become an organization for the younger men in surgery, that is, for those who have completed a fairly long term of service in training and including a residency in surgery. Such men having had an excellent surgical education and background are in a position to make worth-while contributions to the advance of surgery. During recent years the number of such men adequately prepared has increased tremendously. This has been due both to the desire for advanced training, a desire greatly stimulated by both the American College of Surgeons and the American Board of Surgery, and to the increased facilities for such training because of the increase in the number of acceptable residencies now available. However, for such well-trained young men, the opportunities to present the results of their original work at the meetings of any of the already existing surgical organizations have been far too few. Such a young man has

was evacuated almost daily and large quantities of the drug placed in the tissue space. The finally persistent organism was invariably a non-hemolytic streptococcus. Thus, we were confronted with the problem of getting rid of an organism which is commonly found in open granulating wounds, normally of no particular consequence but in the above type of case, a killer, because of clot digestion and secondary hemorrhage.

If the sulfonamide drugs are incapable of eradicating certain low-grade organisms as, for example, the green streptococcus from a blood clot, the success of suture anastomosis of arteries in this war will depend, as before, upon accurately placed sutures without strangulation tension which will preclude extravasation of blood.

If it is conceded that postoperative thrombosis or secondary hemorrhage is the result of a low-grade infection along the line of anastomosis in a sutured artery, it is hard to conceive that anticoagulants are going to have any remarkable influence upon the final outcome. Their early use during a suture anastomosis would complicate hemostasis and favor a residuum of blood clot along the suture line, an open invitation to infection in a contaminated wound.

All good surgeons, with care to well-known details, can generally claim the reward of primary healing of contaminated wounds of the soft parts. They are likewise acutely aware of the problems of repair peculiar to special organs or tissues. The re-establishment of circulation through an important artery that has been severed in a war wound puts up to the surgeon a problem as tedious and difficult as any he may be called upon to solve. Following débridement of the ends of a severed artery in a contaminated wound, primary healing after suture anastomosis is dependent upon several important factors. We have already referred to the danger of residual hemorrhage about the anastomosis. The necessity of placing sutures regularly, not more than $1\frac{1}{2}$ mm. apart, for control of hemorrhage places a serious strangulation threat upon the tissue encompassed and strangulation of tissue invites infection in the contaminated wound. Our pioneers in vascular surgery early recognized this danger and introduced fine Chinese silk. This suture material, because of its low tensile strength, has been cursed, no doubt, by the surgeons unaccustomed to its use but by this very virtue spares tissue from strangulation necrosis when encompassed by closely spaced sutures.

This brings us to a discussion of an important factor which, if not properly evaluated, will doom to failure a well-performed arterial anastomosis, namely, tension. In end-to-end suture of an artery the anastomosis is subjected to tension from two sources, (1) pressure of the blood being forced through the vessel; (2) longitudinal tension due to the elastic recoil of the artery.

The following experimental observations made by one of us (A. H. B.) suggests that the degree of tension may be an important factor in the

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE SEVERED PRIMARY ARTERY IN THE WAR WOUNDED

A NONSUTURE METHOD OF BRIDGING ARTERIAL DEFECTS

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I. The Problem of Suture Anastomosis of Arteries in the War Wounded

MODERN warfare furnishes in profusion wounds of all the different tissues and organs in the body. The rarity of certain of these injuries in civil life naturally leaves us unprepared to handle them as well as we should like, in wartime. In no special type of injury has this been more true than in the case of wounds of the primary arteries of the human body, arteries upon whose patency the life of vital organs and limbs may depend.

It is true that successful junction of arteries by suture and even vein transplants had been made some years before the outbreak of World War I, yet the sad commentary by Sir George Makins¹ on the results of arterial suture during the late War is a warning of the responsibilities we face at the outset of World War II.

There are several questions that naturally arise in connection with the immediate problem of treating war injuries to arteries. First, why has arterial suture failed so miserably during wartime? Second, have there been any advances in science during the interval of peace, that may be expected to contribute favorably to the outcome of cases of arterial injury in the present emergency? The quick answer by many² to these two questions will be that we have the problem of arterial injury under control for this War, a thought that was no doubt entertained by many concerning the expected success of arterial suture before the last World War.

It is easy to say categorically that failure of arterial suture during the last war was due to infection and thrombosis and now that we have the sulfonamide drugs and the anticoagulants, heparin and dicoumarin, the problem is solved. Unfortunately, the situation is not so simple. From an experience with five cases of aneurysm we have learned that there is no sulfonamide in use at this time that will sterilize a blood clot in continuity with the lumen of an artery. In some of the cases the clot

of the arteries have assumed a state of retraction that is more difficult to overcome but, worse yet, a not inconsiderable portion of the ends of the artery must be sacrificed by débridement. The above facts bring up the serious question whether direct end-to-end anastomosis should ever be attempted.

All things considered, it is our opinion that a graft of vein anastomosed end-to-end with the severed artery offers the best chance of successful re-establishment of circulation in a primary artery that has been severed by a war missile. Leakproof anastomoses eliminate the hazard of residual blood clot and this will permit free action of the sulfa drugs at least in controlling the activity of the common pyogenic organisms. A vein graft would eliminate longitudinal tension, a most serious threat to an anastomosis under these circumstances. A vein graft presumably has its mechanism for nourishment intact from the start and will be exposed to an abundance of arterial blood. The one and only serious objection to the use of a vein graft under circumstances of war is the fact that we are totally dependent upon the difficult, tedious, and time-consuming method of suture anastomosis of vessels.

II. The Problem of Collateral Circulation Following Ligation of the Damaged Primary Artery in the War Wounded

There were approximately 4,400 soldiers in the U. S. Army who lost one or more extremities during the last world war.³ Upon discussing the subject with surgeons active in the war we gathered the impression that a good percentage of these amputations were performed because of damage to the blood supply. The decision of when to amputate was one of the most difficult decisions that the surgeon was called upon to make, difficult because the decision had to be made early, preferably before the blanket of traumatic edema had obscured the development of an uncontrollable infection. It required rare clinical judgment indeed and courage of one's convictions to say a given case had sufficient collateral blood flow to ride out a post-traumatic edema and stay the development of a lethal infection. Needless to say, the dilemma quickly and rightly resolved in favor of saving the life of the soldier by adopting a policy of early amputation in such cases.

What will be the policy in this war? Certainly if the results obtained from treating wounds with the sulfonamide drugs during the Pearl Harbor catastrophe can be even approximately duplicated during the rest of this war, our policy will be radically changed.

It is our opinion that the use of the sulfonamide drugs in conjunction with careful débridement and careful hemostasis with the evacuation of blood clot will, for the first time in the history of wars, enable the surgeon to safely postpone amputation in cases of ligated primary arteries until the adequacy or inadequacy of the collateral circulation can be established beyond the peradventure of doubt. With the absence

healing of vessel anastomoses in the presence of bacterial contamination. It was observed in the performance of carotid jugular anastomoses in dogs that primary healing of the wound and the anastomosis could be obtained in the end-to-end variety, i.e. the proximal end of the carotid to the proximal end of the external jugular vein in the presence of slight bacterial contamination. Whereas, using exactly the same routine "aseptic technique," the performance of the side-to-side carotid jugular anastomosis was regularly followed, on or before the ninth postoperative day, by a breakdown of the anastomosis. Routine success with primary healing at the site of the anastomosis in the side-to-side variety was obtained only after the adoption of a more rigid technique of bacterial exclusion.

An explanation of these different results can best be made on the basis of tension upon the vascular anastomosis. In the end-to-end anastomosis the factor of longitudinal strain is entirely eliminated, the artery and vein have been cut entirely across and allowed to retract. The factor of intravascular strain has been reduced also to the point, in fact, that the artery and vein at the point of anastomosis are seen to collapse during cardiac diastole. This great reduction in pressure is due to the fact that the artery suddenly empties its blood into a large neck vein subject to negative pressure within.

One has only to view the vessels to appreciate the greater tension in the side-to-side anastomosis. Here we have arterial blood at high pressure bucking the return of venous blood at the site of the anastomosis. In contaminated cases the side-to-side dogs' wounds heal with primary union except for the vessel anastomosis. The latter apparently does well until the ninth day, then as regularly as clockwork one of two things will happen. Either the dog will suddenly bleed to death because of a breakdown of the anastomosis or, if the fistula is very small, thrombosis will develop. In either case, a culture taken from the line of anastomosis and incubated from five to seven days will likely reveal bacterial growth, usually a nonhemolytic streptococcus.

Whereas these experiments in themselves do not preclude the successful anastomosis of severed arteries in the human being, for that has been accomplished, they do emphasize a narrow margin of safety in the factor of tension upon a vascular suture line. With these experimental facts in mind it is pertinent to note that most of the successful, direct end-to-end anastomoses of arteries have occurred in civil life directly following stab wounds. These wounds are relatively clean and entail little or no sacrifice in the length of the artery. In contrast, during a war arteries are usually severed by a tumbling, ragged missile that macerates as it lacerates. Often many of the potential collateral vessels have also been injured or will be quickly put out of function by traumatic edema. The wounds are contaminated and prone to infection. The wounded come late to the surgeon for arterial anastomosis. The ends

Such a policy in this war would logically lead to a higher per cent incidence of gangrene per primary artery involved.

There will be cases in which prompt treatment of shock and elimination of vasospasm will afford a wide margin of safety for the limb. In other cases post-traumatic edema will so compromise collateral flow and obstruct venous return as to make the outcome dubious for a time.

There will be cases in which, because of laceration of some collateral vessels and confusion to others, it is only reasonable to suppose that the outcome may be favorably influenced by the prevention of thrombosis by the use of an anticoagulant in conjunction with the above measures.

Finally, it must be conceded, in this war as in wars before, there will be a considerable number of cases in which nothing short of the re-establishment of blood flow through the primary artery, if only during the period of post-traumatic edema, will suffice to save the extremity. This will be particularly true of injuries to the popliteal artery.

III. The Chances of Success of a Nonsuture Method of Arterial Anastomosis in This War

Since ancient times the cry for a quick and simple method of anastomosing arteries has risen with every war. Attempts were made by the ancients to bridge defects in arteries by tubular structures such as goose quills and chicken bones. Whereas we have long been aware of the factors that doom such methods to failure, to date we have not been able to eliminate or control these factors.

A nonsuture method of establishing continuity in an artery, to be simple and practical, predicates the use of a supportive tubular structure of some kind. To maintain blood flow through an artery joined in this manner involves: (1) the prevention of clotting, immediate or delayed, (2) the avoidance of infection, (3) the prevention of pressure necrosis of the artery which in turn may cause hemorrhage or late thrombosis.

Certainly, to those of us who have painstakingly learned the technique of suture anastomosis and have experienced the gratification of a well-earned success, even the contemplation of such gross devices of arterial anastomoses are offensive. But the fact remains that suture anastomosis of arteries in the war wounded is by and large impractical, and we are at war!

It is of interest that during the last World War Tuffier⁴ was able to maintain blood flow through a paraffined silver tube, bridging an arterial defect for as long as ten days in one case. In general this is exceptional, according to Makins¹ who states that . . . "as a rule the tube should be removed at the end of four days and at this date I have always found it occluded." It is an interesting commentary however, that Makins looked upon the Tuffier tube as a useful instrument in some cases.

of infection and septic thrombosis the slogan will change from "Save a Life" to "Save a Limb." The responsibility for establishing or encouraging and maintaining an adequate flow of blood will be placed squarely up to the surgeon.

Sir George Makins¹ collected a series of cases during World War I in which the primary arteries had been ligated because of injury and the fate of the extremity left to the collateral blood flow. The percentage of cases complicated by anemic necrosis or gangrene, according to arteries involved were as follows: Carotid artery, 33.33 per cent; subclavian, 25 per cent; axillary, 16.6 per cent; brachial, 23 per cent; femoral, 25 per cent; popliteal, 41.66 per cent. Excluding the carotid, averaging the other arteries, gangrene of the extremities occurred in 26 per cent of the cases.

It is true we have made important advances in the promotion and maintenance of collateral blood flow following obstruction to a primary artery. We know the importance of quickly reviving and maintaining an adequate level of systemic blood pressure in cases of blood vessel injury; we believe our solution to this will be the use of dried plasma or serum albumin on the field.

Conceding that the use of mechanical devices to promote collateral blood flow will be impractical, we have the following measures to offer the soldier with a primary artery injury at the front:

1. Immediate and effective treatment of shock.
2. The use of the sulfonamide drugs to forestall infection.
3. Chemical section of the sympathetic nerve supply to the affected extremity.
4. The use of an anticoagulant (heparin or dicoumarin) to prevent thrombosis in such cases as have laceration or contusion of the collateral vessels as well.

Considering the general policy of early amputation prevailing during World War I when the adequacy of the circulation to an extremity was in doubt makes it fair to assume that the cases reported in Sir George Makins' series were favorable cases. It is our opinion that if in an identical series the first three measures of treatment outlined above were carried out, the incidence of gangrene would approximate 5 per cent instead of 26 per cent as reported by Sir George Makins.

Assuming that we may cut the incidence of gangrene to 5 per cent in favorable cases such as reported by Sir George Makins, what can we postulate, if in this war we find it is safe to defer amputation and give the collateral circulation a chance in all cases of injury in which the primary artery of the extremity has been ligated? It is reasonable to expect that a higher percentage of limbs will be saved. On the other hand, making a practice of deferring amputations routine would include cases involving varying degrees of injury to the collateral vessels as well, a group which in World War I was treated by early amputation.

METHODS

Several different techniques (Figs. 1, *A* and *B*, and 2 *A*) were attempted before a satisfactory method was discovered. In brief, the suture of the divided carotid (or femoral) artery over a vitallium tube* was successful in only one out of nine experiments and in the successful one blood flow was demonstrated for only five days (Fig. 1*A*). Bridging a gap with a vitallium tube by the ligature technique (Fig. 1*B*) was also most disappointing (none out of six). Finally, the bringing of each end of the divided artery through a vitallium tube and bridging the gap with a vein transplant was successful in only two cases out of seven (Fig. 2*A*).

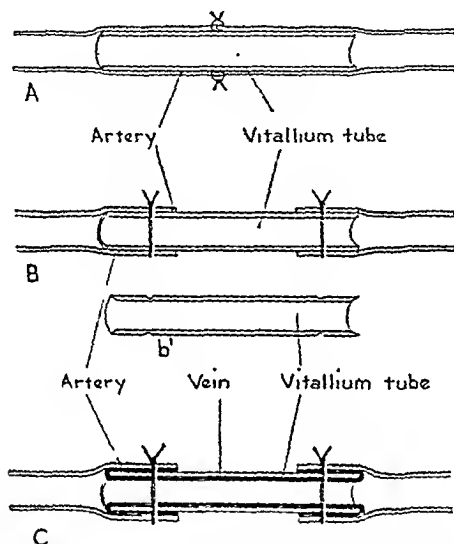


Fig 1—In these drawings are depicted the different methods of using a single vitallium tube. *A*, The artery is sutured in the usual manner over a straight vitallium tube. *B*, the divided ends of the artery are approximated near each end of the vitallium tube by ligatures. In this way a gap is bridged. *C*, the final technique which was highly successful. The drawing shows the vein to be inside the vitallium tube, the ends of the vein are everted over the vitallium tube and the artery is drawn over each end and held by a ligature. In this way the flowing blood contacts only an intimal lined tube.

After the above failures a technique was established of bridging a gap in an artery which functioned fairly well in the small femoral artery and with uniform success in the abdominal aorta for an indefinite length of time (Figs. 1*C* and 2*C*). Dogs have been used as the experimental animals and silk technique was used throughout. No anti-coagulant was employed. Vitallium tubes 2.5 cm. long with an outer diameter of 3 mm. and an inner diameter of 2 mm. have been used as a permanent prosthesis for a vein transplant. The operation is carried out as follows (Fig. 3). The femoral artery and vein of the dog are located and isolated for distances of 7 to 8 cm., each branch being ligated close

*The Austenal Laboratories, Inc., Chicago, Ill., supplied us with the vitallium tubes used in these experiments and we wish to thank Mr. J. J. Erdmann of that company for his cooperation.

At the start of this war we have at our command two effective anti-coagulants, heparin and dicoumarin. It is reasonable to suppose that if proper use were made of these substances, the hazard of early thrombosis may be largely, if not completely, eliminated.

Infection, even if of a low-grade character, as a cause of early necrosis with secondary hemorrhage or thrombosis in an anastomosed artery is well known to all. It is hoped in this war that the sulfonamide drugs, when combined with careful débridement and hemostasis, may largely eliminate the hazard of infection.

If it proves possible that early thrombosis and infection can be prevented in this war for the first time in history, a simple nonsuture method of arterial anastomosis will at least have a chance for success, since it is conceded that these factors have been largely responsible for early thrombosis in previous attempts.

What can be done about factor three, namely, pressure necrosis of the vessel, a cause of late thrombosis in a nonsuture method of arterial anastomosis? As previously stated, the simplest nonsuture method of arterial anastomosis requires the use of a supportive tube or tubes. The unyielding, supportive tube will of necessity be in a pressure relation to the vessel. Two important questions arise: (1) Will it be possible to minimize the effect of the tube upon the vessel to the point of preventing late stenotic fibrosis or thrombosis? (2) If not, would the operation serve any good purpose?

The answer to the first question will be discussed, at least in part, under Results. But certainly we have an abundance of evidence to show that collateral vessels develop *pari passu* with gradual occlusion of a primary artery, and if there were a late thrombosis the only injury done would be to the pride of the surgeon performing the anastomosis. In the case of the soldier with a severed primary artery of the arm or leg, the anastomosis would serve to bridge that dangerous period of post-traumatic edema, the exact extent of which, in a given case, no surgeon can accurately foretell. We have all witnessed, at one time or another, the strangulation of a good collateral circulation by edema. It is known that blocking of the sympathetic innervation in such cases is of little or no avail. Elevation of the leg to relieve edema merely converts the fear of a wet gangrene to the certainty of a dry gangrene. The only measure that could possibly save such a limb would be the prompt re-establishment of a pulsating flow of blood through the primary artery. This would permit elevation of the limb and quick subsidence of edema.

The problem of pressure necrosis by a foreign body introduced to support a ligature anastomosis must be overcome by the use of a material disposing least to infection and interfering little with healing or with the normal physiology of the vessel. Vitallium* more nearly meets these requirements than any other substance available.

*The approximate composition of Vitallium is cobalt 65 per cent, chromium 20 per cent, and molybdenum 5 per cent.

secondly, so that tissue juices released by the very tight ligatures cannot escape into the circulation. After the above has been completed the proximal rubber-shod clamp is released first in order that air bubbles will be driven peripherally. Immediately after release of the distal rubber-shod clamp the blood courses freely and a strong pulsation can be felt distal to the vitallium tube.

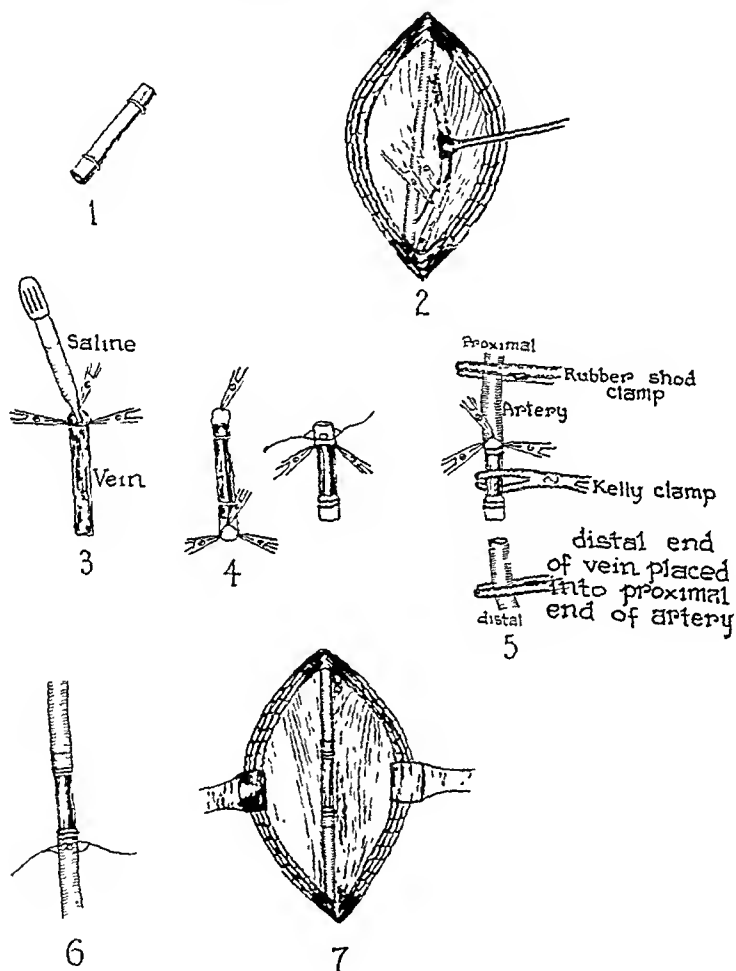


Fig. 3.—The various steps in the operation as carried out in the femoral artery. 1, The vitallium tube with its two ridges (sometimes grooves). 2, Shows the artery and vein exposed; the vein is retracted and clamps have been placed upon a branch. We now think it is perhaps better technique to ligate the branch first, clamp distally, and cut between. 3, The segment of vein upon removal is irrigated with saline solution through a blunt-nosed eye dropper. 4, The vein has been pushed through the inside of the vitallium tube; the two ends are everted over the ends of the tube and are held in place with one or two ligatures of fine silk. 5, The distal end of the segment of vein is placed into the proximal end of the artery and held there by two ligatures of fine silk; all ligatures are placed behind the ridges. 6, The snug ligature near the end of the vitallium tube for the apposition of the artery and vein is being tied. 7, The completed operation showing the femoral artery; a gap of 2 cm. has been bridged.

to the vein with arterial silk and loosely to the artery with fine silk. The segment of vein, 7 cm. long, is then excised between suture ligatures and promptly irrigated with saline solution through a blunt-nosed eye dropper. The distal end of the vein is identified so that it will be brought into approximation with the proximal end of the femoral artery, allowing blood to flow through the graft in the direction of the valves. One end of the vein is then pushed through the inside of the vitallium tube and the ends of the vein are everted over the tube for 1 cm. at each end. A single tie of fine silk near each end holds the vein in place. The tie is placed some 8 to 9 mm. from the end of the tube. Care is taken from this point to allow nothing to touch the exposed intima of the vein and it is frequently moistened with saline solution. The femoral artery is then divided after rubber-shod clamps have been applied. The ends

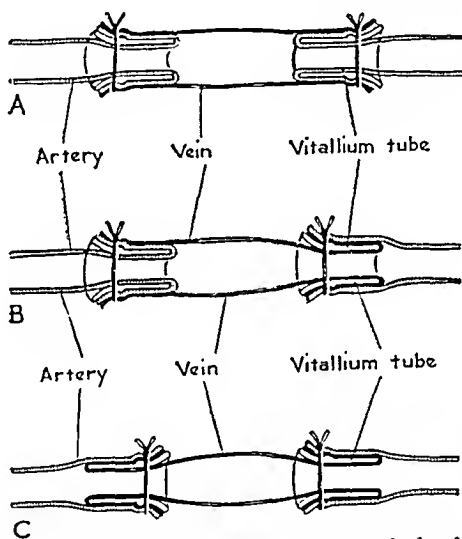


Fig. 2.—In these drawings are depicted the different methods of using two vitallium tubes in combination. *A*, The divided ends of the artery are brought through each vitallium tube and everted; a ligature holds the everted artery in place; a vein transplant is then brought over each vitallium tube and held with ligatures. *C*, The vein is brought through each vitallium tube and the everted ends held in place by ligatures. The ends of the divided artery are brought over the vitallium tube and held in place by ligatures; this method makes it possible to bridge a gap of any length, the limiting factor being the length of the vein transplant. *B*, A combination of the methods shown in *A* and *C*.

of the artery are irrigated with saline solution and with three mosquito clamps each end of the artery is brought over the vitallium tube lined with vein for the distance of 1 cm. The ends of the artery are fastened to the tube beyond the ridges with two ties of fine silk at each end (Fig. 1*C*). This maneuver results in the intima of the artery being in contact with the intima of the vein for 6 to 8 mm. Finally, a tie of fine silk is tied loosely over the artery at each end, 1 to 2 mm. from the end of the vitallium tube, so that blood cannot penetrate between the two intimas (Fig. 4) and hence, form a thrombus in the first place, and

secondly, so that tissue juices released by the very tight ligatures cannot escape into the circulation. After the above has been completed the proximal rubber-shod clamp is released first in order that air bubbles will be driven peripherally. Immediately after release of the distal rubber-shod clamp the blood courses freely and a strong pulsation can be felt distal to the vitallium tube.

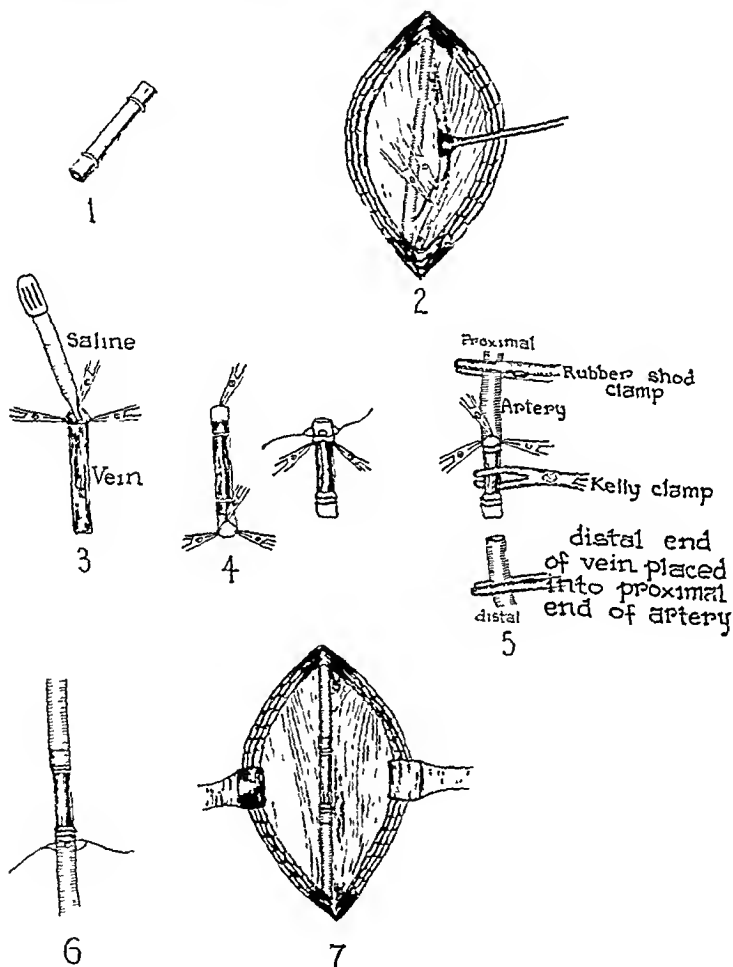


Fig. 3.—The various steps in the operation as carried out in the femoral artery. 1, The vitallium tube with its two ridges (sometimes grooves). 2, Shows the artery and vein exposed; the vein is retracted and clamps have been placed upon a branch. We now think it is perhaps better technique to ligate the branch first, clamp distally, and cut between. 3, The segment of vein upon removal is irrigated with saline solution through a blunt-nosed eye dropper. 4, The vein has been pushed through the inside of the vitallium tube; the two ends are everted over the ends of the tube and are held in place with one or two ligatures of fine silk. 5, The distal end of the segment of vein is placed into the proximal end of the artery and held there by two ligatures of fine silk; all ligatures are placed behind the ridges. 6, The snug ligature near the end of the vitallium tube for the apposition of the artery and vein is being tied. 7, The completed operation showing the femoral artery; a gap of 2 cm. has been bridged.

A modification of the above procedure has been made for the use of longer gaps in an artery. Two vitallium tubes with funnel ends are handled in a similar fashion to the above method (Fig. 2C).

RESULTS

1. Femoral Artery.

1. *One-tube Technique* (Fig. 1C).—Nineteen femoral arteries have been operated upon and the artery explored at intervals postoperatively. No anticoagulant was used. There are four ways to determine the patency of the operative site, two of the methods being presumptive and the other two conclusive. The first presumptive method is to palpate the femoral artery distal to the vitallium tube and if a good pulsation is present, at least equal to that noted immediately postoperatively, then the anastomosis may be patent. The second method is to inject diodrast

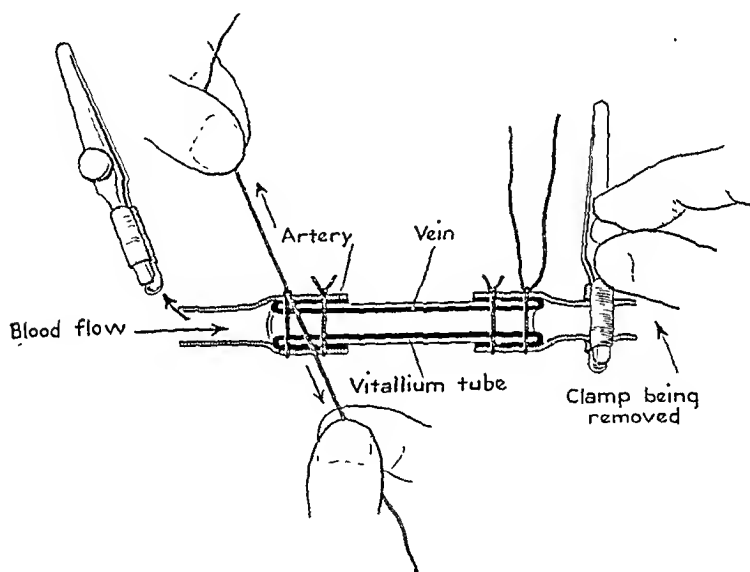


Fig. 4.—Illustrating the tying of the snug ligature near the end of the vitallium tube. This ligature prevents blood from penetrating between the two intimas and also keeps any tissue juice freed by the crushing ligature from escaping into the general circulation.

into the abdominal aorta and if the dye can be seen in the femoral artery above and below the vitallium tube, then conclusive evidence is obtained as to the patency of the anastomosis (Fig. 5). On the contrary, if no dye is seen to pass through the operative site, patency may still exist (Fig. 6). The two conclusive methods of determining the patency of the operative site are, (1) the operative isolation of the femoral artery proximal and distal to the vitallium tube, ligation of all nearby branches, and then with a rubber-shod clamp on the distal end, insertion of a needle into the artery between the clamp and the tube and (2) the demonstrable patency of the anastomoses at autopsy.



Fig 5A.

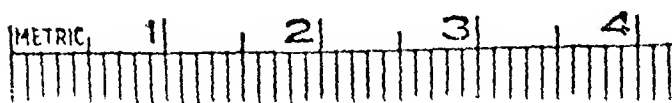
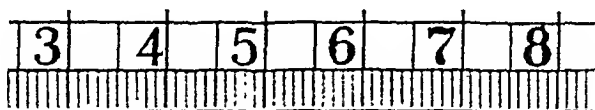


Fig 5B

Fig 5—A, Diodrast injection of the abdominal aorta in animal No 1862 shows the right femoral artery to be entirely patent, the left side, however, is blocked some 8 to 9 cm above. This x-ray was taken sixty-nine days postoperatively. B, The specimen from the right femoral artery showing minimal reaction around the vitallium tube and the silk ties to have remained in place, complete healing has occurred between the intima of the vein and that of the artery at each end.

In Table I the two columns refer to the presumptive and conclusive evidence regarding the patency of the arterial anastomoses. It is interesting to note that in some of the animals, that is, No. 1827, no pulsation could be felt over either artery while at exploration the following day the right artery was patent. The reverse of the above experience is not unusual, i.e. No. 1838.

Of the nineteen femoral arteries, six were proved patent by exploration and three at autopsy. Of the ten failures, some of these occurred before all ten points in the technique to be described below had been worked out and in one case obvious tearing of the segment of vein occurred during the eversion of it over the vitallium tube. Finally, several of the arteries may have been patent during the first postoperative week as judged by strong pulsation, only to thrombose at a subsequent time.



healed junction
of artery and vein

Fig. 6.—The photograph shows the opened specimen of the left femoral artery where excellent healing has taken place between the intimas of the artery and vein. The vitallium tube has been removed and the vessel is entirely patent, this having been demonstrated by sectioning the artery distal to the anastomosis. It is interesting, however, that a diodrast injection made just before the animal was sacrificed failed to demonstrate patency.

2. *Two-tube Technique* (Fig. 2C).—This method was used in three instances and at exploration two of them were proved patent. In the third case the animal died and a clot, presumably post-mortem, was found in the segment of vein (Table II).

II. Abdominal Aorta.

Because of the extremely small lumen of the femoral artery (2 to 3 mm.) it was necessary to use a vitallium tube only 3 mm. in its outer diameter. Such a tube had an inner diameter of only 2 mm. and after the segment of vein had been drawn through the vitallium tube the lumen of the segment was approximately 1.5 mm. It is obvious that

TABLE I
FEMORAL ARTERY, ONE TUBE TECHNIQUE

NO. OF DOG	FEMORAL ARTERY	ASSUMED TO BE PATENT BY PALPATION	PROVED PATENT
1855	Left side	+(1)	+(2) Died and autopsy
1862	Right side		+(5) +(19) +(69)
	Left side		+(5) +(19) +(33) -(69) All exploration
1827	Right side	-(4)	+(5) Explored
	Left side	-(4)	-(5) Explored
1859	Right side		+(3) Explored
	Left side		-(3) Explored
1806	Right side (tearing)		-(14) Explored
	Left side		+(14) Explored
1838	Right side	+(1) +(22) +(47)	-(49) Explored and diodrast
	Left side	+(1) +(22) -(47)	-(49) Explored and diodrast
1842	Right side		+(2) Died and autopsy
	Left side		+(2) Died and autopsy
1880	Right side	±(7)	-(35) Exploration O K,
	Left side	±(7)	+(35) diodrast failed
1915	Right side	+(7)	-(11) Died from hemorrhage
1906	Right side	-(1) -(5)	-(15) Exploration and diodrast
	Left side	-(1) +(5)	-(15) Exploration and diodrast
1920	Right side	-(4)	-(6) Explored

+ Pulsation or patency of vessel

- No pulsation or occluded

The numbers in the parentheses refer to the postoperative day on which examination was made

TABLE II
FEMORAL ARTERY, TWO TUBE TECHNIQUE

NO OF DOG	FEMORAL ARTERY	ASSUMED TO BE PATENT BY PALPATION	PROVED PATENT
1855	Right side	+(1)	+(2) Died and autopsy
1854	Right side	-(5)	+(6) At exploration
	Left side	-(5)	+(6)

+ Pulsation or patency of vessel

- No pulsation or occluded

The numbers in the parentheses refer to the postoperative day on which examination was made

such arteries are not comparable to those in human beings in which this method might find applicability, arteries such as the popliteal, femoral, and brachial which have diameters more nearly approximating that of the dog's aorta below the renal vessels. For that reason we have used the one- and two-tubed techniques with inner diameters of 5 mm. in the abdominal aorta of five dogs and patency has been proved in three of them on the third, sixteenth, and twenty-seventh postoperative days and presumed on the fourth and first postoperative days of the remaining two animals (Fig 7). A segment of jugular vein has been employed for the transplant to the abdominal aorta. A good femoral pulsation between 50 and 75 per cent of the preoperative pulse pressure (estimated

roughly by palpation) is observed immediately postoperatively and daily palpation of the femoral arteries has proved to be an excellent index of the patency of the aorta at the operative site. Table III shows



Fig 7—A, A flat plate of the abdomen shows the two vitalium tubes to lie over the fourth, fifth, and sixth lumbar vertebra. B, Diodrast injection of the abdominal aorta above the operative site shows complete patency of the vein transplant. Careful examination reveals that the width of the diodrast as it emerges from the lower vitalium tube is as broad as that above the proximal vitalium tube.

the data on the anastomoses in the abdominal aorta and although the experience is brief, the operation has been simple to perform and the uniformity of the results are encouraging. In one of the dogs (No. 1908) ribbon catgut was used as the snug ligature employed to appose the two intimas at each end and whereas at fourteen days the femoral arteries were pulsating vigorously, two days later they had diminished

somewhat. Exploration and diodrast injection revealed patency of the anastomosis (Fig. 8) but blood had dissected between the intimas of the proximal ends of the artery and the vein transplant with the formation of a small retroperitoneal hematoma; in addition, beginning thrombosis was noted at the proximal end. The explanation of this occurrence is to be found in the fact that the ribbon catgut had been digested by the fourteenth day and could not be identified at operation two days later. In the other three dogs No. 13 silk was used for the ligatures.



FIG. 7B.—For legend see opposite page.

Other animals are being subjected to operation using the one- and two-tube techniques in the abdominal aorta and will be observed at

longer intervals in order to determine the ultimate efficacy of the method. It is worthy of note that the vitallium tubes we have employed in the abdominal aorta have a diameter of only one-half that of the abdominal aorta and more nearly approximate the diameter of the average human popliteal artery. The inference is therefore obvious, that if the procedure is successful in the abdominal aorta of the dog, then the likelihood of success is even greater in the popliteal artery of man where such disproportion does not exist.



Fig 8 —Diodrast injection of the aorta above the vitallium tube shows a faint stream to have passed through the tube down each external iliac artery

TABLE III
ABDOMINAL AORTA

NO. OF DOG	TYPE OF TECHNIQUE	ASSUMED TO BE PATENT BY PALPATION	PROVED PATENT
1885	One-tube technique	+(27)	+(27)
1908	One-tube technique	+(14) +(16) weak	+(16) Beginning thrombosis
1955	One-tube technique	+(2)	Not yet examined
1924	Two-tube technique	+(3)	+(3)
1936	Two-tube technique	+(5)	Not yet examined

+ Pulsation or patency of vessel.

The numbers in the parentheses refer to the postoperative day on which examination was made.

DISCUSSION

Analysis of these experiments furnishes nothing conclusive as to the permanency of the nonsuture method of arterial anastomosis presented. In fact, a considerable number of the experiments entailed the use of vitallium tubes in a way which we knew beforehand could not maintain the patency of the artery, but were done to study the healing of vessels in contact with vitallium, the effect of tension, etc.

There is little doubt that many of these same anastomoses may have been kept patent for indefinite periods by the use of a few milligrams of dicoumarin daily. In our experiments without the use of anticoagulants, it became apparent that arrangements (Fig. 1C, a vein-lined Tuffier tube, and ends of vein graft Fig. 2C) everted over two short, flanged vitallium tubes were best, the latter preferable for bridging large arterial defects.

During the development of the method certain technical points arose. These, fortunately, have in no way affected the simplicity of the procedure and are based upon principles well known to surgeons. They are as follows:

1. Avoidance of longitudinal strain upon the anastomosed artery beyond physiological limits. This requires a segment of vein which measures roughly (before removal) three times the length of the arterial defect to be bridged when a $2\frac{1}{2}$ cm. tube is to be used. For a 5 cm. vitallium tube, the segment of vein should be 10 cm. or longer.

2. A wound free of blood and tissue juices. Careful hemostasis and frequent irrigation with physiologic saline solution will largely attain this condition.

3. Avoid the use of crushing clamps upon the vessels. In the preparation of the vein graft the branches should be ligated almost flush with the vein by a ligature of arterial or No. A braided silk; the branch is then clamped distally and cut. To remove the vein graft, ligate first distally (empty the vein of blood), then proximally with a noncrushing ligature, quickly remove the graft, irrigate, and place it in saline solution. The stumps of the vein remaining in the body are then further secured by means of transfixion sutures.

4. The vein graft, after one end is pushed through the inside of the vitallium tube, is everted over the ends of the tube or tubes (Figs. 1C or 2C) and tied beyond the ridges. Care is taken to prevent the exposed intima from contacting anything until it is ready to be inserted into the ends of the artery.

5. After division of the artery between rubber-shod clamps the divided ends are irrigated with saline solution and the intima freed of clinging particles of fibrin and excess adventitia.

6. Care is taken to be sure that the proximal end of the artery is anastomosed to the distal end of the vein graft because of the venous valves.

7. The ends of the artery are brought over the ends of the vein which have been everted over the supporting tube or tubes (Figs. 1C or 2C) and are tied with a strong ligature which is retained from slipping by a ridge on the vitallium tube (Fig. 3).

8. This brings us to the seemingly critical point of a nonsuture method of artery anastomosis; namely, what happens to the anastomosis when the securing ligatures necrose through the vessel walls? The broad contact between the intima of the vein and that of the artery, in addition to being a safeguard against thrombosis, affords a large healing surface. The avoidance of tension, both longitudinal and circular, in this area subjects the vessel walls to a minimal disturbance of their own nutrition. Circular tension is best avoided by the simple precaution of selecting a vitallium tube (or tubes) no larger in diameter than the cut ends of the artery.

A relatively thin-walled tube of the proper size with the vein graft everted over the ends results in an inconsequential degree of narrowing at the site of anastomosis in a sizable artery. It has been demonstrated that the area of the lumen of an artery may be reduced to 50 per cent without any change in the volume of blood flow through the artery.⁵ The rate of blood flow at the constricted area is of necessity increased, which in itself would be an additional safeguard against thrombosis at the site of anastomosis.

It is true that a vitallium tube too small would permit the ends of the artery to fit loosely and would expose the method to a serious threat. When blood is permitted to flow through such an anastomosis, it works its way up over the ends of the tube between the intimas of the vein and artery. Here a relatively stagnant film of blood usually clots when met by a descending film of clot stimulating tissue juice which has been squeezed out between the intimas by the tightly placed retaining ligatures. The result is that a ring of red thrombus quickly presents itself at the narrowest point of the anastomosis where, in spite of the rapid blood flow, a varying degree of white thrombus becomes deposited upon the red thrombus. If the artery is small to begin with and the tube yet smaller, the inevitable result is complete occlusion, usually within forty-eight hours.

Control of the above hazard is quite simple. Immediately after the retaining ligatures are set, two good-sized ligatures of soft braided silk are passed around each arterial cuff at a point well away from the necrosing ligature and about 1 to 2 mm. from the end of the vitallium tube which is approximately 1 cm. within the artery (Fig. 4). The first part of the knot is tied loosely in both instances. Flow through the anastomosis is established by an assistant while the operator immediately tightens the ligature over the proximal end of the tube just sufficiently to approximate snugly the intimas of the artery and vein. The knot is completed quickly and the ligature on the distal tube similarly tied.

9. Trapped air bubbles within the vein graft should be made to pass on. This can be accomplished almost invariably by releasing the artery proximal to the anastomosis first. In case this should fail, elevation of the extremity with gentle milking of the vein in case of the two-tube technique, will suffice.

10. Finally, the vessel sheath should be closed snugly over the anastomosis. Clotting of serum quickly takes place around the anastomosis and vein graft and

the fibrin network later is invaded by fibroblasts forming a supportive mold. The adhesions thus formed between the ends of the artery and the vessel sheath help to prevent displacement after the necrosing ligatures have cut through.

SUMMARY AND CONCLUSIONS

A nonsuture method of arterial anastomosis was advanced under the hypothesis that the use of the sulfonamide drugs and possible use of anticoagulants will afford in this war, for the first time in the history of wars, a basis for success of such a method.

It was further postulated that a nonsuture method of arterial anastomosis capable of maintaining patency of the primary artery in an extremity beyond the period of post-traumatic edema would in all probability, with the aid of other well-tested measures, save the extremity from gangrene.

We have presented the results of preliminary experiments in twenty-seven arterial anastomoses in dogs in which no anticoagulant was employed in order to estimate the basic value of the method.

Ten points of technique were discussed as being important to the success of, but not complicating the simplicity of, the nonsuture method of arterial anastomosis.

We have demonstrated that a segment of vein lives when used within a vitallium tube in the manner described to bridge an arterial defect. The mechanism of its nutrition is a problem under current study.

The results upon the small femoral arteries of dogs without the use of anticoagulants would seem to justify a hopefulness for its clinical success where the arteries may be many times larger. This optimism is further abetted by the results in the five instances of the use of the method in the abdominal aorta of dogs. Circulation was intact on the first, third, fourth, sixteenth, and twenty-seventh days respectively.

The study should be continued in conjunction with contused lacerations of the arteries with contamination, carrying out the anastomoses with and without the use of the sulfonamide drugs locally. Recent researches on the use of the anticoagulant dicoumarin suggest further study of anastomosis of arteries in conjunction with this drug. Heparin emulsified in oils has been quoted as giving four times the duration of effect when given in the bone marrow.⁶ The subcutaneous route has been described recently as an effective method for prolonging the effect of heparin.⁷ These drugs should be standardized in terms of the amount required to maintain the flow of blood in injured arteries as well as the method of administration.

Aside from the psychologic factor when the young soldier is maimed for the rest of his life by the loss of a limb, there is an enormous economic factor which when put on an actuarial basis reveals the rather startling fact that an amputee costs the government several times more than the payment of a death benefit. Records of hospital admissions during World War I, show that there were 12,000 deaths and 4,403 amputees in the United States Army. Of the 4,403 amputees⁸ only 690

were traumatic amputations, leaving a group of 3,713 surgical amputations.⁹ Granting that the majority of the operations were performed for gas gangrene and seriously infected comminuted compound fractures, a significant percentage of the operations were carried out because an injury to the major artery of the extremity had occurred. The 4,403 amputees cost the United States government over \$100,000,000 as against \$120,000,000 for the entire group of 12,000 men who died in hospitals. When one realizes that there were approximately 300,000 amputees¹⁰ of all countries in the last war, then the vital importance from the economic point of view of reducing the number of amputations by a simple method of restoring the main arterial blood flow becomes evident.

GENERAL SUMMARY

I. Aspects of suture anastomosis of injured arteries in the war wounded are discussed in relation to the use of sulfonamide drugs and anticoagulants.

II. The significance of the use of the sulfonamide drugs in cases of primary artery injury in relation to amputation is discussed.

A change of policy regarding amputation in cases of severed primary arteries is postulated. The importance such a policy would place upon the problem of collateral circulation is discussed. Practical methods of improving and maintaining collateral circulation including the use of heparin and dicoumarin are emphasized.

III. The great need for a simple, quick method of joining arteries together in wartime is emphasized.

The basic factors upon which a successful nonsuture method of anastomosis must depend are discussed.

Results of preliminary experiments in the dog, using the vitallium tube as a supportive structure for nonsuture anastomosis of arteries, are reported.

REFERENCES

1. Makins, G. H.: Gunshot Injuries to the Blood Vessels, England, 1919, John Wright & Sons, Ltd.
2. Pratt, G. H.: Importance of a Knowledge of Vascular Surgery in World War II, *Am. J. Surg.* 56: 335, 1942.
3. Ireland, M. W.: Medical Department of the U.S. Army in the World War, vol. 11, Washington, D. C., 1927, War Department, U.S. Government Printing Office, p. 719.
4. Tuffier, M.: L'Intubation Arterielle, *Bull. Acad. de méd.*, October, 455, 1915, *Bull. et mém. Soc. de chir. de Tome, Mareh*, 43, 1917.
5. Mann, F. C., Herrick, J. F., Essex, H. E., and Blades, E. J.: Effect on Blood Flow of Decreasing Lumen of Blood Vessels, *SURGERY* 4: 249-252, 1938.
6. Macht, D. I.: Absorption of Drugs Through the Bone Marrow, *Proc. Soc. Exper. Biol. & Med.* 47: 299-302, 1941.
7. Loewe, L., Rosenblatt, P., and Lederer, M.: A New Method of Administering Heparin, *Proc. Soc. Exper. Biol. & Med.* 50: 53, 1942.
8. Ireland, M. W.: Medical Department of the U.S. Army in the World War, vol. 11, Washington, D. C., 1927, War Department, U.S. Government Printing Office, p. 719.
9. Ireland, M. W.: Medical Department of the U.S. Army in the World War, Medical and Casualty Statistics, vol. 15, part 2, Washington, D. C., 1925, War Department, U.S. Government Printing Office, p. 1017.
10. Ireland, M. W.: Medical Department of the U.S. Army in the World War, vol. 15, part 2, Washington, D. C., 1925, War Department, U.S. Government Printing Office, p. 713.

Review of Recent Meetings

MEETING OF THE CENTRAL SURGICAL ASSOCIATION, CHICAGO, ILL., FEBRUARY 27 AND 28, 1942

THE Second Annual Meeting of the Central Surgical Association was held Feb. 27-28, 1942, at Chicago, Ill., with headquarters at the Drake Hotel.

Most of the papers presented at this meeting are to be found in this issue of SURGERY. Those not included are as follows:

J. A. Sill (by invitation) and James M. Winfield, Detroit: The Use of Bile in the Therapy of Certain Surgical Lesions.

William S. Keith, Toronto: Empyema of the Spinal Epidural Space.

Because the authors are in military service, the following papers were read by title only.

Donald M. Glover, Cleveland: Experimental Cross Grafting of Skin.

Harvey S. Allen, Chicago: Treatment of Burns.

Thomas C. Douglass, Chicago: Volvulus of the Small Intestine.

Frank E. Stinchfield, New York: The Evaluation of Internal Fixation of Fractures of the Lower Extremity of Tibia and Fibula.

Philip Shambaugh, Chicago: Clinical Studies on the Prevention of Postoperative Pulmonary Complications.

Frank Lounsbury (by invitation) and Michael L. Mason, Chicago: Tensile Strength Following Suture of Denervated Tendons.

J. Harold Couch, Toronto: Bilateral Preganglionic Sympathectomy for Raynaud's Disease With Gangrene of the Fingers.

Paul Greeley, Chicago, in a discussion of the paper on the effect of topical application of several substances on the healing of cutaneous wounds by Brush and Lam,^{*} reported experiences similar to Dr. Lam's in the local use of chemicals to hasten wound healing. He stressed the harmful effects of allowing extensive scarring and fibrosis to occur in such wounds and recommended early skin grafting even though the cosmetic result may not be perfect and later regrafting may be necessary.

In closing, Lam mentioned the great number of substances offered as a panacea for all wounds and stated that at the Henry Ford Hospital there was a standing offer to try any substance that comes along on twelve guinea pigs with adequate controls. He called attention to the large number of substances recommended for clinical use without experimental studies having been made.

Eugene A. Osius, Detroit: Appendicitis in the Tuberculous Patient.—A report was made of the study of 103 cases of surgically treated appendicitis occurring in patients with pulmonary tuberculosis. The following conclusions were drawn: (1) The symptoms and signs of appendicitis in patients with pulmonary tuberculosis are essentially the same as those of the nontuberculous patient, (2) the diagnostic problem is often made difficult by the protean manifestations of tuberculosis both pulmonary and abdominal, (3) tuberculous involvement of the appendix is frequently unrecognized, (4) the mortality of appendicitis in patients

^{*}See page 355 for article by Brush and Lam.

with pulmonary tuberculosis is markedly influenced by tuberculous involvement of the appendix and adjacent structures, (5) appendicitis without tuberculous involvement has no effect on the pulmonary infection, and (6) in general, tuberculous involvement of the appendix indicates a widespread infection.

Roscoe R. Graham, Toronto, in discussing the paper, related some of his experiences with tuberculous appendicitis. He suggested that when a patient is supposedly suffering from appendicitis with a mass, if this mass diminishes in size but does not disappear under conservative treatment despite a return to normal of pulse and temperature, one is not dealing with ordinary pyogenic appendicitis. In such cases, the possibility of a tuberculous infection should be considered. Leon J. Leahy, Buffalo, N. Y., inquired if Dr. Osius had excluded from his series, cases in which there were obvious peritoneal tubercles. Henry J. Vandenberg, Grand Rapids, inquired regarding the incidence of tuberculous involvement of the cecum in these cases. James K. Staek, Chicago, asked about the mechanism of death in these patients. Osius, in closing, stated that he had not excluded tuberculous peritonitis in this series of cases. He believed that when there is a mixed pyogenic and tuberculous infection of the appendix, the organ should be removed in order to prevent the danger of a fatal general peritonitis. In two of the patients with postoperative fecal fistulas, the appendical stump was only tied but not inverted. Since that time he has inverted the stump, paying particular attention to the toilet of the stump. He stated that there was involvement of the cecum in many of the cases studied; in others, the ileum alone was involved while in some there was a generalized infection of the abdominal cavity. Among the more important causes of death were advance of the tuberculous process, general peritonitis, and liver abscesses.

Lawrence Sidney Fallis, Detroit: **The Use of the Mikulicz Resection in Carcinoma of the Right Colon.**—The author defined the indications for one-stage resections of the right colon with primary suture anastomosis, for the two-stage procedure, and for the Mikulicz type of operation for lesions in this segment of the colon. The latter type of operation he felt was of great service in that group of patients whose condition is only fair because of loss of weight, anemia, or mild obstruction, and in the unprepared patient. He cited among the advantages of the Mikulicz procedure the low primary mortality, the avoidance of operative decompression in the presence of obstruction, and the fact that the tumor is removed at the first operation. The inconvenience of the temporary ileostomy was not regarded as of great significance and while there are two periods of hospitalization, the total hospital stay is not greater than that of the two-stage method.

George E. Wilson, Toronto, in a discussion of the paper, said that he believed the Mikulicz operation to be an excellent procedure in very advanced cases where infection of the tissues immediately surrounding the growth is present. In general, he preferred to do a resection with primary anastomosis in one stage and advocated the use of the Furniss clamp. Charles H. Mead, Duluth, emphasized the applicability of the Mikulicz type of operation to the small intestine when dealing with obstructing lesions, such as strangulated hernias. Fallis, in closing, stated that he believed that after twenty-four or thirty-six hours, there has been enough sealing off of the tissues about the bowel ends to prevent spread of infection and, therefore, the clamp may be released, thereby overcoming the acute obstruction. In his technique the tumor is not resected until after the wound is closed and the dressings applied, a method which minimizes the danger of peritonitis. When doing the one-stage operation, he recommended an end-to-side anastomosis using the end of the colon to the side of the ileum because this makes a safer anastomosis.

In a discussion of the paper by Szilagyi, Brush, and Harkins,* on their clinical experiences with the McVay herniotomy, Kellogg Speed, Chicago, inquired whether there was danger during the operation of injuring the lymph node of Rosenmüller which lies high in the femoral canal. Such injury might possibly spread infection through the operative field. J. Dewey Bisgard, Omaha, inquired if difficulty was ever encountered in approximating the aponeurosis of the transversalis to Cooper's ligament. He had found in some cases of large direct hernias that a flap of pectineus fascia could be elevated and then sutured without tension to the transversalis or the conjoined tendon. Harkins, in closing, explained that he had sometimes used a relaxing incision in the internal oblique and transversalis aponeurosis after lifting up the external oblique aponeurosis rather than taking a flap from below.

In the discussion on the report made by Miller† of 230 cases of subtotal gastric resection for peptic ulcer. Henry Harkins, Detroit, asked Dr. Miller to discuss further his eleven cases of perforated ulcer for which gastric resection was done and to outline, in his opinion, the indications for gastric resection in acute perforation. Roseoe Graham, Toronto, briefly reviewed his experiences in the treatment for perforated duodenal ulcer by the method of simple closure with an omental graft. There were five deaths in ninety-six consecutive cases. In a follow-up study of sixty-eight patients treated by this method, only thirty-five later had trouble sufficient to require consideration of further operation and only sixteen of these were operated upon. Symptoms in the others were controlled by conservative measures. Since acute perforations of peptic ulcers must be treated frequently by surgeons of relatively little experience, he believed it to be a dangerous teaching to advocate anything more than the simplest operative procedure compatible with saving life. M. G. Gillespie, Duluth, mentioned the common causes of death in gastroduodenal surgery. In his opinion these are: (1) leakage at the suture line, (2) disturbances of the emptying of the resected stomach, and (3) pulmonary complications such as atelectasis or some complication of atelectasis. As preventive measures, he suggested: (1) the reinforcing of all suture lines with silk; (2) continuous infusions of saline, glucose, and blood during the operative procedures; and (3) routine aspiration of the larynx, trachea, and bronchi. A. D. McLachlin, Toronto, related his experiences with the method of tracheobronchial suction described by Cameron Haight. In his cases this method had been eminently successful in the prevention of serious postoperative complications. He stressed the importance of early treatment and of repeated aspirations when necessary. In closing, Miller supported Dr. Graham's plea for very thorough training for those who wish to do gastric surgery. He felt that simple closure of acute perforations may sometimes be unsuccessful since these ulcers represent an acute process and the process may continue and cause re-perforation. The mortality of simple closure as recorded in the literature ranges from 15 to 50 per cent. In his twelve cases of acute perforation treated by resection, only one patient died, a mortality of 8 per cent. He did not advocate resection as a routine method for the treatment of perforated ulcer but on his service performs this operation in cases arriving at the hospital within twelve hours following the perforation. He mentioned the technical difficulties encountered in the closure of the stump of the duodenum in these acute cases when resection is performed. His experience had been different from that of Dr. Gillespie in that leakage at the suture line had not been the source of trouble. He recommended the insertion of two purse-string sutures at the angle between the gastroduodenal stoma and the closed portion of the stomach as suggested by Finsterer. In edema of the stoma, gastroduodenal siphonage

*See page 364 for article by Szilagyi, Brush, and Harkins.

†See page 383 for article by Miller.

with blood, plasma, and saline infusion, together with adequate vitamins, is an important adjunct in treatment. In his series, this complication was not the cause of death in any case. He believed that atelectasis was the principal cause of postoperative pneumonia. At the present time he favors spinal anesthesia and the use of a rebreathing bag used several times a day. A very simple dressing for the wound is used in order to insure free movement of the lower chest. In his series there were no deaths from pneumonia. To prevent pulmonary embolism, the patients routinely do so-called bicycle leg exercises as soon as they are able. With regard to bleeding, he considers two types, i.e., gross and massive. Patients with gross hemorrhage which stops almost immediately are treated medically until they fully recover. The cases of massive hemorrhage in patients under forty-five years of age are treated conservatively, if possible, for forty-eight hours. If the bleeding does not stop then, operation is carried out. In patients over forty-five years of age, operation is performed within twenty-four hours if bleeding is progressive. He reported eleven cases of really massive hemorrhage operated upon (resection in ten cases) with no deaths.

Clifford D. Benson, Detroit: Surgical Excision of Primary Tumor of the Liver (Hamartoma) in Infant Seven Months Old With Recovery.—A case of a large tumor of the liver in a 7-month-old infant was described. At operation, a primary tumor of the liver was found and treated by excision. The patient made a satisfactory recovery and the microscopic study of the tissue proved the lesion to be a hamartoma of the liver.

A. F. Jonas, Jr., Omaha: Post-Traumatic Strictures of the Intestine.—Benign strictures of the small and large intestine were classified as follows.

- A. Congenital
- B. Following intensive irradiation
- C. Following ulcerating infections
 - 1. Tuberculosis
 - 2. Syphilis
 - 3. Gonorrhea
 - 4. Amebiasis and other dysenteries
 - 5. Regional enteritis
 - 6. Lymphopathia venereum
- D. Chemical and thermal
- E. In the aged (?), vitamin deficiency
- F. Following vascular injuries
 - 1. Replacement of a strangulated hernial loop
 - 2. Ligature of middle colic or other artery
 - 3. Mesenteric thrombosis or infarction
 - 4. Trauma to mesenteric blood supply

Two cases of benign stricture of the intestine following abdominal trauma were reported. Such strictures may be associated with a pernicious anemia-like syndrome which disappears following appropriate surgical correction. Various technical procedures for the treatment of these lesions were considered.

Charles W. McLaughlin, Jr., Omaha, discussing obstructions of the second and third portions of the duodenum as described by Zinninger's article,* called attention to the clinical syndrome of chronic duodenal ileus and mentioned the frequency of associated persistent attacks of migraine.

Arthur R. Metz of Chicago reported good results in the treatment of obstructions of the distal duodenum due to pressure by the mesenteric vessels by gastroenterostomy and occlusion of the pylorus by heavy double silk ligatures. He believed that this is a simpler procedure than duodenojejunostomy. He also mentioned the ease with which moderate obstruction of the duodenum may be overlooked during the roentgenologic examination.

*See page 393 for article by Zinninger.

Bernard B. Larsen, Ohio, reviewed his experiences with cases of duodenal obstruction and advised a conservative plan of treatment. In general, he felt that the results of surgical therapy were disappointing.

Bernard B. Larsen, Cleveland: **A Simplified Method for Inserting a Smith-Petersen Nail in Intracapsular Hip Fractures.**—This subject was presented as a moving picture, demonstrating a newly developed guide in a simplified technique for inserting a Smith-Petersen nail in intracapsular fractures of the hip. The procedure is most easily done under fluoroscopic control, but may also be used with x-ray plates alone.

An initial skin incision is not made. A Steinman pin is placed along the anterior mid-portion of the femoral neck, a guide block is threaded on this Steinman pin, and then a trocar is passed through the guide and against the femoral shaft. The sheath of the trocar acts as a guide through which the guide wire for the Smith-Petersen nail is drilled into position. A small incision, just large enough to admit the nail, is made and the nail is driven home. The advantages claimed for the procedure are its speed, minimal shock to the patient, absence of bleeding, decreased chance of infection, and accuracy in placing the nail.

During the discussion Edward Parnall, Minot, N. Dak., asked how the fragments were impacted in order to insure union.

George Hammond, Ann Arbor, asked if difficulty had been encountered in breaking the outer femoral cortex by the insertion of the nail.

Kellogg Speed emphasized the importance of primary complete reduction and of proper aftercare. He also believed that the method of treating fractures of the neck of the femur by plaster fixation should not be discarded in our teaching.

In closing, Larsen stated that the driving of the nail into place seemed to secure adequate impaction. He also stated that difficulty had not been encountered in breaking the cortex when the guide wire into the femur was placed not too far down upon the shaft and stated that the proper place is about one inch below the most prominent portion of the greater trochanter. In concluding, he stressed the simplicity of this procedure and the absence of serious complications in his experience with it.

George E. Wilson, discussing the article on the use of sulfonamides in the treatment of compound fractures, by C. Leslie Mitchell,* mentioned the fact that Colonel Kirk of the Walter Reed Hospital, Washington, administers sulfanilamide orally to injured soldiers and then subsequently carries out the usual débridement with excellent results. Dr. Wilson had had good results by the method advocated by W. H. Ogilvie of London, that is, by leaving all compound fractures wide open without any attempts at suture. He pointed out that one cannot tell by the condition of the patient whether a wound is doing well or not when sulfathiazole has been placed in it and in some instances infection is thus overlooked. Ralph C. Carothers, Cincinnati, mentioned the value of relaxation incisions in order to allow comfortable skin closure of the primary wound. Primary split thickness skin grafts are useful in covering the relaxation incisions. Willis J. Potts, Oak Park, Ill., cited his experience with osteomyelitis secondary to compound fractures treated by plating or wiring immediately after the injury. He raised the question of the propriety of the use of such foreign bodies in wounds which cannot be closed. A. W. Farmer, Toronto, stated that he had used skin grafts in compound fractures extensively with good results. He recommended the use of skin grafts to the primary wounds or the use of relaxation incisions with a direct pedicle shift and skin grafting of the second wound. In closing, Mitchell cited experimental work

*See page 403 for article by Mitchell.

with blood, plasma, and saline infusion, together with adequate vitamins, is an important adjunct in treatment. In his series, this complication was not the cause of death in any case. He believed that atelectasis was the principal cause of postoperative pneumonia. At the present time he favors spinal anesthesia and the use of a rebreathing bag used several times a day. A very simple dressing for the wound is used in order to insure free movement of the lower chest. In his series there were no deaths from pneumonia. To prevent pulmonary embolism, the patients routinely do so-called bicycle leg exercises as soon as they are able. With regard to bleeding, he considers two types, i.e., gross and massive. Patients with gross hemorrhage which stops almost immediately are treated medically until they fully recover. The cases of massive hemorrhage in patients under forty-five years of age are treated conservatively, if possible, for forty-eight hours. If the bleeding does not stop then, operation is carried out. In patients over forty-five years of age, operation is performed within twenty-four hours if bleeding is progressive. He reported eleven cases of really massive hemorrhage operated upon (resection in ten cases) with no deaths.

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*See page 393 for article by Zininger.

should be followed carefully by repeated clinical examinations. If any change in the character of the lesion develops, it should be considered malignant and histologic proof of its innocence is essential

Walter G. Maddock, Ann Arbor, inquiring about the paper by Barker and Priestley,* on postoperative thrombophlebitis and embolism, asked the speaker (1) the differentiation of thrombophlebitis and phlebothrombosis, (2) his opinion of peripheral venograms in the search for the origin of an embolus, (3) his opinion of the use of ligation of the femoral or iliac vein as a prophylactic measure against pulmonary embolism

W. E. Abbott, Cleveland, inquired if the speaker believed that dicoumarin acted by its effect on the prothrombin level in the blood and if there was evidence of decreased liver function from the use of the drug.

G. Gavin Miller inquired if, at the time of ligation of the femoral vein above a peripheral thrombosis, it is advisable to suck out the thrombus from the iliac vein

In reply, Barker stated that the studies to date indicate that dicoumarin produces its effect entirely by inhibiting the formation of prothrombin, this action probably taking place in the liver. He emphasized the importance of regulating the dose of dicoumarin for each patient on the basis of daily determinations of the prothrombin level. Contrary to expectations, there is no evidence in human beings or animals that even large doses will produce organic changes in the liver. Renal insufficiency was given as a contraindication to the use of dicoumarin. As it is possible, but not certain, that the drug is eliminated through the kidneys, it has been observed that it is more difficult to stop the effect of the drug when renal insufficiency is present than when it is not. He warned against giving dicoumarin to patients who already have a deficiency of prothrombin. The effect of dicoumarin is not immediate and it may be two or three days before adequate elevation of the prothrombin time is obtained after administration of the drug has begun. Likewise, the effect may persist for as long as ten days after administration of the drug has been discontinued. The only way one can restore the prothrombin time to normal is by the transfusion of fresh extracted blood. He stated that he did not believe thrombophlebitis and phlebothrombosis were two separate diseases but rather stages or variants of the same process and that an attempt to divide cases into these two categories tended to confuse rather than clarify the problem. The speaker stressed the fact that organization of a thrombus takes place rapidly and usually within twenty-four hours, or almost certainly within seventy-two hours. It becomes firmly adherent to the wall of the vein. Hence, it does not seem probable that an embolus occurs as a result of dislodgment of a thrombus or a portion of a thrombus which has been present in a vein for a very long period. If embolism occurs after clinically evident thrombophlebitis is present it occurs as a result of detachment of a new thrombus which may be a sudden extension into a more proximal vein, or perhaps the thrombus has formed in an entirely different vein, possibly in the other extremity. As important evidence, he mentioned the fact that if one examines fatal pulmonary emboli histologically, no evidence of organization of the margins of these emboli is seen, which suggests that the embolus did not exist as a thrombus in the vein for a very long period. He did not favor ligation of the femoral or iliac veins because he did not think that there is much chance of accomplishing the desired effect thereby. However, should it be done, he believed the vein should be opened and as much as possible of the thrombus sucked out of the vein. He stated that there is no assurance that thrombosis will not develop proximal to the point of ligation and the ligature will certainly not prevent thrombosis from developing in the opposite extremity.

*See page 411 for article by Barker and Priestley.

which indicated that sulfanilamide powder used locally is far more effective than the oral administration. He believed that under the conditions of war the wound in compound fractures usually should be left open. In general, in his series, there was a higher incidence of infected wounds when some form of internal fixation was used than in those cases in which it was not employed.

Cameron Haight, Ann Arbor: in a discussion of Siler's* paper on acute costal chondritis associated with sternal osteomyelitis re-emphasized the seriousness of infection of the costal margin; once it becomes infected, it is necessary to remove the entire costal margin in order to effect a cure. The reason for this is the poor blood supply. He pointed out the possibility of infection of the costal margin from infected lymph nodes along the internal mammary chain. Since infection in one costal margin may extend to the xiphoid and then to the opposite side, he suggested that it might be well to do a clean operation near the xiphoid, thus interrupting the continuity of the costal margin in a clean field and thereby preventing extension. Siler, in closing, discussed the question of whether the fifth and sixth cartilages touch and said that he believed sufficient detailed anatomic studies had not yet been made to answer this question.

George Hammond, Ann Arbor: Elevation of the First Metatarsal Bone With Hallux Equinus.—Forty-two examples of elevation of the first metatarsal with hallux equinus were reviewed. The modes of production, methods of prevention, and operative correction of the deformity were considered.

The deformity is caused by a muscular imbalance of the foot which is the result of various primary diseases. An imbalance of muscles acting upon the first metatarsal caused the deformity in 86 per cent of the cases, while 14 per cent were the results of muscular imbalance of the great toe.

The primary disease was anterior poliomyelitis in 64 per cent of the examples. Tendon transference accounted for the deformity in 70 per cent of the cases in this group (45 per cent of the total series). Before transference of the peroneus longus tendon careful consideration should be directed to the effect of such transference upon the first metatarsal. This tendon should not be transferred to the region of insertion of the anterior tibial tendon nor should it be transferred to the os calcis without regard for a strong anterior tibial muscle.

The results of operative correction of this deformity had been relatively good.

Cameron Haight, Ann Arbor: Congenital Atresia of Esophagus With Tracheo-esophageal Fistula.—The pathology of congenital atresia of the esophagus with tracheo-esophageal fistula was reviewed and a brief résumé of the literature pertaining to this subject was given. A detailed report of such a case treated by operative repair was presented. This patient made a good recovery from the operation, and had been followed for nearly one year.

James W. Logie, Ann Arbor: Mastopathia Cystica and Carcinoma of the Breast.—A survey of the literature was made and resulted in considerable evidence to support either a casual or causal relationship between mastopathia cystica and mammary carcinoma. Mastopathia cystica was found histologically in 67 or 57 per cent of 118 specimens from cases of carcinoma of the breast treated by radical mastectomy. In sixteen of these cases, or 13.5 per cent, the carcinoma appeared to be arising in the area of mastopathia cystica. This degree of association cannot be expected through chance distribution. The highest incidence of mastopathia cystica was found in patients in the decade of 40 to 50 years, whereas the incidence of carcinoma continued at the same high level for the next three decades. Once the diagnosis of mastopathia cystica is made, the patient

*See page 407 for article by Siler.

A series of fifty amputations was reported in which the mortality rate was 12 per cent. Extensive use of conservative treatment prior to amputation had been employed. In a survey of the deaths of this series the importance of surgical judgment was stressed. Nondrainage of closed amputation wounds was thought dangerous, especially for the surgeon of limited experience. In extensive organic arterial occlusion, minor amputations were almost always unsuccessful and greatly increased the risk incurred in secondary major amputations. It was concluded that the operative risks involved in major amputations should not be greater than that for other major operations performed upon patients of advanced age with extensive arteriosclerosis.

In discussing the paper, George E. Wilson inquired if Dr. Theis would resort to conservative treatment in diabetic gangrene in which pulsation in one of the vessels of the foot was present. He believed it to be a useful procedure.

In closing, Theis stated that there were no instances of amputation where one of the ankle arteries was not occluded and that conservative treatment was successful where the vessels were incompletely occluded. He mentioned the fact that in his reported series ethylene anesthesia was used in almost every case.

Russell C. Hanselman, Chicago: **Experimental Shock: Hemorrhage.**—The speaker presented experimental data obtained from the production of shock in dogs by hemorrhage. The following alterations in the physical and chemical properties of the blood were noted: (1) the sedimentation rate is probably increased beyond the amount accounted for by the lowered red blood count; (2) the white blood count showed a rise with a terminal fall; (3) the hematocrit paralleled the red blood count fall; (4) when the cell volume, the cell hemoglobin, and cell hemoglobin concentrations are considered it was found that the cell size in cubic microns decreased as hemorrhage progressed; (5) the cell hemoglobin and cell hemoglobin concentration increased; (6) the blood specific gravity did not decrease as rapidly as either the red blood count or the hematocrit; (7) the plasma proteins paralleled the specific gravity of the plasma; (8) blood chlorides showed a slight decrease; (9) blood sugar showed an increase; (10) the N.P.N. varied only within the normal range, with a slight upward trend; (11) the serum sodium decreased with hemorrhage; (12) the blood and serum potassium increased; (13) the calcium decreased; (14) magnesium increased; (15) inorganic phosphorus rose sharply with the onset of shock; and (16) moderate inorganic acidosis occurred.

The respiratory rate showed much individual variation and no characteristic change. The animals died after a blood loss equivalent to 4 to 5.5 per cent of the body weight had occurred.

Jacob Berman, Indianapolis, in discussing the paper by Power, Pedersen, and Maddock,* on their clinical experience with sodium chloride replacement therapy, stressed the importance, when supplying fluids, of making sure that they would be retained by the capillaries. For this purpose protein and oxygen are necessary. When large quantities of saline solution are given, the osmotic pressure is lowered and the hydrostatic pressure increased thus permitting the loss of fluid into the tissue spaces. Thus, it becomes necessary to study the blood chloride, hematocrit, and plasma protein when a patient is being maintained on intravenous fluids. It is the compensatory mechanisms which permit the introduction of 1,000 c.c. of normal saline solution into the circulation without regard to the hypochloremia which may or may not be present. Thus, 9 Gm. of salt are introduced into the circulation. If needed it is retained, if not, water is attracted into the blood stream and sodium and chloride are lost in the urine. In certain disease states

*See page 435 for article by Power, Pedersen, and Maddock.

In a discussion of the paper on aspiration bronchopneumonia by Apfelbach,* Stuart C. Cullen, Iowa City, asked the speaker if he could give an estimate as to the minimal amount of contamination which the average patient could withstand. W. H. Cassels, Chicago, called attention to the fact that many patients have gross contamination of the tracheobronchial tree from aspiration and yet do not develop extensive bronchopneumonia. Often suction by means of a catheter will remove much of this material. The fatal cases of aspiration of gastric contents are usually in patients who are debilitated. In concluding, Apfelbach explained that the condition which he had described is due to the fact that the aspirated gastric content contains a high concentration of hydrochloric acid and is rich in bacteria; the serious lesions are the result of this combination rather than being due to either the chemical effect or the bacterial content alone.

Harry G. Hardt, Jr., Chicago: Comparison of the Course and Direction of Fatal and Nonfatal Gunshot Wounds of the Chest.—A comparative study was made of one hundred patients who expired within twelve hours after being shot in the chest and of one hundred patients who recovered from penetrating gunshot wounds in this region. In the fatal cases profound hemorrhage was a constant finding usually due to injury of the heart aorta or large mediastinal vessels. The majority of the wounds of entrance in both groups were located on the anterior thoracic wall and in the fatal group they were practically confined to the mid-chest and the left lower anterior region. A comparison of these two groups in cross section of the chest revealed that the fatal wounds crossed the mediastinum in practically every instance while the nonfatal wounds rarely entered the mediastinum. Comparison of the vertical angles of the wounds of both series showed no demonstrable differences. Protection of the chest with some type of bullet-resisting material from the episternal notch above to the sixth interspace below, and from a point 5 cm. to the right of the right border of the sternum to the left anterior axillary line, would have prevented sixty-four wounds of the anterior chest in the fatal series.

George M. Curtis, Columbus, Ohio, in a discussion of the paper on familial hemolytic jaundice by McLaughlin, Jr.,† called attention to the genetic significance of congenital hemolytic icterus and suggested the term "genetic hemolytic icterus" for this disease. Considering the genetic background, he reported a case of splenectomy performed upon an infant 53 days of age, presumably, the youngest patient upon whom splenectomy had been successfully performed for an acute hemoclastic crisis. He pointed out that if a mother is splenectomized, she will later bear children who will have the same disease and conversely, the splenectomized father can beget children with the disease.

In concluding, McLaughlin warned against errors in diagnosis and attempts at correcting the lesion of the biliary tract before taking care of the spleen since there is danger of precipitating a crisis with the immediate and urgent demand of performing a splenectomy soon after the operation upon the biliary tract. He stated that he did not believe that the increase of red blood cells and hemoglobin occurring during splenectomy were due to hemoconcentration. He called attention to the leg ulcers often present in this disease; their treatment consists in eradication of the primary disease.

Frank V. Theis, Chicago: Amputations for Advanced Arterial Disease; A Critical Analysis of the Mortality.—A clinical study was conducted in order to determine whether delay in performing major amputations increased the mortality.

*See page 413 for article by Apfelbach.

†See page 419 for article by McLaughlin.

A series of fifty amputations was reported in which the mortality rate was 12 per cent. Extensive use of conservative treatment prior to amputation had been employed. In a survey of the deaths of this series the importance of surgical judgment was stressed. Nondrainage of closed amputation wounds was thought dangerous, especially for the surgeon of limited experience. In extensive organic arterial occlusion, minor amputations were almost always unsuccessful and greatly increased the risk incurred in secondary major amputations. It was concluded that the operative risks involved in major amputations should not be greater than that for other major operations performed upon patients of advanced age with extensive arteriosclerosis.

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these substances may be lost into the tissues thus producing edema, not only in the subcutaneous tissues but in the lungs, pleural and peritoneal cavities, and the brain. Therefore, salt replacement therapy should be carefully controlled.

W. H. Cassels, Chicago: *The Surgeon and the Anesthesia Technician*.—The speaker gave the following suggestions to surgeons employing nurse anesthetists: (1) to realize the fact that ethylene and nitrous oxide are not potent anesthetic agents and that deep anesthesia with these agents should not be demanded; (2) to allow ample time for the induction of anesthesia; (3) not to demand extremely deep anesthesia, going beyond the limits of safety; (4) not to deprive the anesthetist of access to the respiratory tract. He stressed the importance of good judgment in the use of preanesthetic medication and of the surgeon being able to recognize and deal with anesthetic emergencies when they arise during the course of the operation.

During the discussion of nonasphyxial nitrous oxide anesthesia from his paper with McQuiston, Stuart C. Cullen* stated that with the relatively heavy medications which they use in nitrous oxide anesthesia and with 20 per cent oxygen supplied to these patients, there is no interference with the cellular oxidation sufficient to interfere with the individual's metabolism.

He said he had expected to receive some comment relative to the effect on the cell of the relatively heavy premedication used in this nitrous oxide anesthesia. It can be argued that in spite of the fact that 20 per cent oxygen is supplied to these individuals, and the arterial blood kept well saturated, the tissue is unable to use it because of the excessive premedication.

They feel, of course, that they are not interfering with the cellular oxidation sufficiently enough to cause temporary or permanent damage.

Jacob Berman thought that the discussions on anoxemia were equally pertinent because even though a patient has ample fluids of all kinds he must have a sufficient amount of oxygen so that this fluid will be retained. In this connection, shock due to hemorrhage must necessarily be treated differently than shock due to burns or other trauma. Plasma is sufficient in the latter to restore normal circulation because there is hemoconcentration, whereas in the former there is, in addition, an anemic anoxemia. Whole blood will be required so that oxygen may be carried to the endothelium and other tissues.

During the present emergency we are all engaged in the organization of first-aid squads. We must constantly emphasize that there are two things we cannot live without—blood and oxygen. No matter how our mechanisms compensate for their deficiencies or for their insults, if there is not available an adequate supply of each, the patient will not survive. A lack of either will produce anoxemia, and one without the other is useless. Therefore, in the care of the injured we must give aid to those who are bleeding and those who are deprived of oxygen first. Every drop of blood counts and oxygen must be available.

Berman said, "I have always taught that ether is by far the safest anesthetic known. However, I believe that it is the man who gives the anesthetic rather than the anesthetic agent which is perhaps most important. Dr. McQuiston has properly evaluated the dangers of anoxemia in surgical anesthesia which can occur with ether as well as nitrous oxide."

McQuiston explained to the group that he and Dr. Cullen are not personally familiar yet with war anesthesia and so did not mention that in the paper. However, it is their understanding that the only inhalation anesthetics that are being used with any frequency in war surgery at the present time are nitrous oxide and ether. Cyclopropane has not yet become popularized in the army hospitals, and because of this emergency which faces us the re-evaluation of nitrous oxide at this time is particularly important.

*See page 459 for article by McQuiston and Cullen.

Norris J. Heckel, Chicago: Sex Hormones.—A study was made on the effect of male and female sex hormones upon the function of the normal testis, the volume of the seminal fluid, and the prostatic gland. Testosterone propionate caused a spectacular drop in the number of spermatozoa due to extensive alterations of the seminiferous tubules. This substance has very little if any effect upon the volume of the seminal fluid. No effect of the male sex hormones upon benign prostatic hypertrophy could be demonstrated. Alpha estradiol benzoate and diethylstilbestrol were also used for similar studies. These two preparations exert the same effect upon the spermatogenic function of the human testis as testosterone propionate. In contrast to the male sex hormone, however, the female sex hormone causes a marked suppression or complete disappearance of the seminal fluid, suggesting that the secretory mechanisms of the prostate gland and seminal vesicles are affected. Diethylstilbestrol was tried in cancer of the prostate with general clinical improvement.

In a discussion of the paper, **Linden Seed, Chicago**, related his experiences in the use of colchicine, a mycotic poison, in its effect upon cancer. There was at first a subsidence of the neoplastic process but later accelerated growth occurred. He pointed out the similarity in formula of the estrogenic hormones and the mycotic poisons. He believed that every carcinogenic agent is also an inhibitory agent to cancer and every inhibitory agent is carcinogenic. He believed that the effect of the estrogenic hormone is probably not hormonal but rather due to its mycotic poisonous effect. Sooner or later a drug should be found in which the inhibitory effect is more marked than the carcinogenic effect.

Kellogg Speed, Chicago: Malignant Degeneration of Neurofibromata, of Peripheral Nerve Trunks (von Recklinghausen's Disease).—This paper was presented to emphasize the dangers of incomplete operations or irritation of these tumors in peripheral nerve. According to the literature, the occurrence of sarcoma in the neurofibroma of peripheral nerves averages from 8 to 15 per cent. Two cases were reported in detail from a series of fifteen instances of von Recklinghausen's disease admitted to the Presbyterian Hospital. The following conclusions were drawn: (1) The development of pain along the course of a peripheral nerve containing a tumor, in a patient with von Recklinghausen's disease, suggests sarcomatous degeneration of the neoplasm; (2) operative removal of a tumor mass involving a peripheral nerve should be very carefully and thoroughly performed since such operative interference may lead to local recurrence or distant metastasis of the tumor; (3) if sarcomatous proliferation is believed to be present, early amputation, if possible, is the best treatment. According to the literature, x-ray therapy is of little value.

Frank V. Theis, in a discussion of the paper, related an unusual experience in which a neurofibroma of the femoral nerve was removed five times. After the fifth removal the patient was given very intensive deep x-ray therapy with apparent complete cure. Recently the patient had returned and roentgen studies of the chest showed a huge intrathoracic tumor which later was removed surgically. Microscopically, the tissue was exactly the same as that in the tumor previously removed from the leg.

In closing, **Speed** emphasized the point that his remarks were concerned purely with sarcomatous degeneration in von Recklinghausen's disease. He pointed out that while the original tumor may seem to remain encapsulated in the original area, distant metastasis is not infrequent.

Edward Parnall, Minot, discussed a method of extensive laminectomy with replacement of removed laminae, as described by **Albert S. Crawford*** in his paper on the

*See page 482 for article by Crawford.

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Book Reviews

Clinical Roentgenology of Pregnancy. By William Snow, M.D., Springfield, Ill., 1942, Charles C Thomas, Publisher.

This brief monograph represents selections from the observations of the author and his associates on the roentgen examination in pregnancy. It is divided into a number of parts. The first encompasses a thorough-going discussion of the technique of roentgen examination. There follows a very brief discussion of the clinical roentgenology of pregnancy. This is scarcely an adequate presentation, although the diagnosis of abnormalities of the fetus and of position are touched upon. The statement that the diagnosis of pregnancy cannot be made roentgenologically before fifteen weeks is in error.

The author presents a relatively simple method of pelvimetry which, while not as accurate as others, may be good enough for general clinical use. This is presented in some detail with directions for the use of the method which are easy to master. The discussion of soft tissue roentgenography for the demonstration of the placenta is adequate. Snow prefers the use of air rather than sodium iodide in the bladder and also in the rectum for contrast. He also uses the lateral view of the abdomen without contrast media. The discussion of the effect of hydramnios on the roentgenogram is very interesting. The final section is comprised of case reports which are well presented and give good illustrations of the value of roentgenography in pregnancy. The bibliography is not elaborate, but is adequate.

The monograph suffers from a rather crude literary style. The use of "x-ray" as a verb, of the term "x-ray picture" and many other such expressions is to be deplored. The information, however, is fundamentally sound and well presented.

1941 Yearbook of General Surgery. Pp. 369. Chicago, 1941. The Year Book Publishers, Inc.

The Year Book of General Surgery has become an indispensable aid to every surgeon who essays to encompass the developments in surgery from year to year. It is essentially a practical book, dealing with helpful new techniques. The source of the material is world-wide in its scope, much of it coming from journals, which do not ordinarily come beneath the surgeon's notice. Numerous editorial comments by Dr. Ewart Graham permeate the whole volume and contribute much to its value. A number of the editorial comments have important historic connotations, affording the reader useful orientation with reference to innovations and usage. It is not an easy task to keep this annual review of surgical literature up to a high standard of excellence, an accomplishment which the editor achieves year after year. The work can be recommended highly, not alone for its instructional value, but as a source book which does not allow the reader's interest to flag.

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the sender. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

INDUSTRIAL SURGERY: PRINCIPLES, PROBLEMS AND PRACTICE. By Willis W. Lasher, M.D., F.A.C.S. Cloth. Price \$6.50. Pp. 472, with 194 illustrations. New York, 1942, Paul H. Hoeber, Inc.

subject. Parnall asked if the speaker had performed any ordinary spinal fusion operations after laminectomy. Crawford, in closing, related his experience in one case where an extensive bone graft from the tibia had been used with recurrence of symptoms one year later. At reoperation, marked overgrowth of bone had occurred and it was this experience, in part, which led him to work out the operation described. He believed that thereby the back should be made nearly as strong, the danger of overgrowth of bone overcome, and operative trauma minimized. He also believed the patient could return to work earlier than the patient with a bone graft.

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Original Communications

INTERNAL WIRING FIXATION OF FACIAL FRACTURES

WILLIAM MILTON ADAMS, M.D., MEMPHIS, TENN.

DUE to the increased number of extensive facial fractures within the last few years, there is an obvious need for a method of treatment of such fractures which may be quickly applied and one which affords complete immobilization. After using numerous types of extraoral appliances, including those attached to plaster headcaps, for immobilizing fractures of the maxilla and other facial bones, the author has found these appliances are complicated, their preparation and application are time consuming, they are cumbersome and uncomfortable for the patient, and they require close watching and repeated adjustments on the part of the surgeon. The fact that practically everyone treating these fractures has a different type of extraoral appliance suggests that this method is not entirely satisfactory.

During the past eight years, we have treated eighty-five fractures of the maxilla. The occurrence of head and other facial injuries with fractures of the maxilla is shown in Table I.

As may be seen, there were three fatalities in this series, all three of the patients having had an associated brain injury. Two died of concussion and contusion of the brain, and the third of cerebral meningitis. All expired before their physical condition would permit manipulative procedures for reduction of the facial fractures.

Until two years ago, some type of extraoral appliance was generally employed in these cases. Since then, open reduction and fixation by wiring of the fractured parts to the neighboring unfractured bony structures have been carried out in all cases wherein immobilization was required, with three exceptions; in these three, open reduction was contraindicated and it was necessary to resort to the use of an extraoral appliance.

Received for publication, May 22, 1942.

THE 1941 YEAR BOOK OF INDUSTRIAL AND ORTHOPEDIC SURGERY. By Charles F. Painter, M.D. Cloth. Price \$3.00. Pp. 480, with 271 illustrations. Chicago, 1942, The Year Book Publishers, Inc.

ROENTGEN TREATMENT OF INJECTIONS. By James F. Kelly, M.D. Cloth. Pp. 432, with 122 illustrations. Chicago, 1942, The Year Book Publishers, Inc.

THE PRINCIPLES OF NEUROLOGICAL SURGERY. By Loyal Davis, M.S., M.D., Ph.D., D.Sc. (Hon.). Cloth. Price \$7.00. Pp. 503, with 298 illustrations. Philadelphia, 1942. Lea & Febiger.

TEXTBOOK OF SURGERY. By Frederick Christopher, B.S., M.D., F.A.C.S. Cloth. Pp. 1764, with 1538 illustrations. Philadelphia, 1942, W. B. Saunders Co.

1941 YEAR BOOK OF GENERAL SURGERY. Cloth. Pp. 356, with 196 illustrations. Chicago, 1942, The Year Book Publishers, Inc.

SURGICAL CLINICS OF NORTH AMERICA. By many contributors. Cloth. About 300 pages, illustrated. Philadelphia, 1942, W. B. Saunders Co.

PEDIATRIC GYNECOLOGY. By Gordon Schauffler, M.D., University of Oregon Department of Medical Science, Portland, Ore. Cloth. Price \$5.00. Pp. 364, with 66 illustrations. Chicago, 1942, The Year Book Publishers, Inc.

HISTORY AND EVOLUTION OF SURGICAL INSTRUMENTS. By C. J. S. Thompson, Royal College of Surgeons, London. Cloth. Pp. 113, with 115 illustrations. New York, 1942, Schuman's.

UROLOGICAL DISEASES OF PREGNANCY. By E. Granville Crabtree, M.D. Cloth. Price \$6.50. Pp. 472, with 384 illustrations. Boston, 1942, Little, Brown & Company.

SURGICAL PHYSIOLOGY. By Joseph Nash, M.D. Cloth. Price \$6.00. Pp. 496. Springfield, Ill., 1942, Charles C Thomas, Publisher.

CARCINOMA OF THE STOMACH. By Waltman Walters, B.S., M.D., M.S., Howard K. Gray, B.S., M.D., M.S., and James T. Priestley, B.A., M.D., M.S., Mayo Clinic and Mayo Foundation, Rochester, Minn. Cloth. Pp. 576, with 141 illustrations. Philadelphia, 1942, W. B. Saunders Co.

THE MANAGEMENT OF FRACTURES, DISLOCATIONS, AND SPRAINS. By John Albert Key, B.S., M.D., Jefferson Hospital, Birmingham, Ala., and H. Earle Conwell, M.D., F.A.C.S., Washington University School of Medicine, St. Louis, Mo. Cloth. Price \$12.50. Pp. 1303, with 1259 illustrations. St. Louis, 1942, The C. V. Mosby Company.

DISABILITY EVALUATION: PRINCIPLES OF TREATMENT. By Earl D. McBride, B.S., M.D., F.A.C.S., University of Oklahoma. Cloth. Price \$9.00. Pp. 631, with 374 illustrations. Philadelphia, 1942, J. B. Lippincott Company.

PATHOLOGY OF THE ORAL CAVITY. By Lester R. Cahn, D.D.S., Columbia University, New York. Cloth. Price \$7.50. Pp. 240, with 165 illustrations. Baltimore, 1942, Williams & Wilkins Company.

THE PRINCIPLES OF ANATOMY AS SEEN IN THE HAND. By Frederic Wood Jones, D.S.C., F.R.S., University of Manchester, Manchester, England. Cloth. Price \$7.50. Pp. 418, with 144 illustrations. Baltimore, 1942, Williams & Wilkins Company.

SURGICAL CLINICS OF NORTH AMERICA. Lahey Clinic Number, Boston, Mass. Cloth. Pp. 974, with 318 illustrations. Philadelphia, June, 1942, W. B. Saunders Co.

MANUAL OF STANDARD PRACTICE OF PLASTIC AND MAXILLOFACIAL SURGERY. By National Research Council: Subcommittee on Plastic and Maxillofacial Surgery, Washington, D. C. Cloth. Pp. 432, with 259 illustrations. Philadelphia, 1942, W. B. Saunders Co.

carried out on both sides at the same time, with special attention to any asymmetry, irregularities, or crepitus.

In fractures of the maxilla with downward displacement, inspection will reveal an elongation of the middle third of the face; if the maxilla has been depressed backward as well, the patient will have a "dish-pan" face, particularly if the nasal bones are also depressed, and the teeth will be in malocclusion.

In any facial injury, one should always determine whether the upper jaw is movable. This is easily accomplished by grasping the upper teeth between the fingers of one hand while supporting the back of the head with the other. Motion may be up and down or from side to side. When up and down, movement of the infraorbital ridges may often be detected. One should also observe whether motion of the lower jaw is limited on opening and closing or in the shift from side to side.

Roentgenograms should be made routinely in the posterior-anterior and lateral views, and should include all the facial bones of both the upper and lower jaws. Some fractures, especially those of the temporomandibular joint, may not be demonstrated in these routine films; when such fractures are suspected, roentgenograms in special views should be made.

Anesthesia.—If the bony fragments are not impacted and reduction is possible by manipulation, the procedure may be carried out under local anesthesia. In more difficult cases a general anesthetic is necessary, the type depending largely upon the skill of the anesthetist. Intratracheal anesthesia and sodium pentothal are both satisfactory, but should be given only by one well-trained in their administration. When there is any doubt as to the choice of the anesthetic, the use of ether by the open method is advisable.

Technique.—After the diagnosis has been made, one should visualize the fractured parts in their architectural relationship to the normal bony structures, without regard to the overlying soft tissues. The treatment then should be relatively simple. The soft tissue wounds should, of course, be treated in the usual manner.

Fractures of the maxilla are rarely encountered alone, rather, they are generally associated with fractures of one or more of the other facial bones, including the mandible. Since the maxilla is the foundation structure, accurate apposition and immobilization of this fracture is of prime importance; once these are accomplished, immobilization of the secondary fracture offers little difficulty.

In carrying out this method of open reduction and fixation of fractures of the facial bones, it is necessary to make an incision at only one or two sites: overlying the infraorbital ridge, or at the lateral margin of the supraorbital ridge, depending upon the bones involved. In the event of a laceration over either of these areas, the wires may be inserted through the wound.

This method not only meets the requirements of facility of operation, complete immobilization, and sound surgical principles, but is applicable to practically every type of fracture of the facial bones. The procedure may be carried out with only a pair of pliers, a small drill and dissecting set, and a spool of fine stainless steel wire. Since complete immobilization is obtained, repeated adjustments are unnecessary and the patient is spared much discomfort and inconvenience. Patients are usually able to resume their activities after the tissues have recovered from the acute stage of the injury and when healing is complete the wires are easily removed. Regardless of how extensive the fractures, immobilization by this method has proved far simpler and more satisfactory than by the use of extraoral appliances attached to plaster headcaps.

TABLE I

DISTRIBUTION OF EIGHTY-FIVE FRACTURES OF THE MAXILLA AND ASSOCIATED INJURIES (1934 TO 1941)

YEAR	NUMBER OF CASES	FRACTURE OF THE MAXILLA	FRACTURE OF THE ZYGOMA	FRACTURE OF THE NASAL BONES	FRACTURE OF THE SKULL	FACIAL LACERATIONS	INFECTION WITH DRAINAGE	DEATHS
1934	4	1				3		
1935	8	3	3		1	6		1
1936	5	1	3	1		3		
1937	4	1	3	1	1	1		
1938	12	2	3	3		9	1	
1939	13	2	3	3	1	10		1
1940	17	2	2	4	1	11	2	1
1941	22	7	5	4	1	17	2	
Total	85	19	22	16	5	50	5	3

Undoubtedly, in the exceptional case, extraoral appliances are essential and therefore should be included in the armamentarium of every surgeon who does this type of work. In the presence of infection, particularly in compound fractures, open reduction is definitely contraindicated. Even here, however, an extraoral appliance may be required only for temporary immobilization; after the infection subsides, one may remove the appliance and wire the fragments together.

The treatment of fractures of the facial bones must, of course, be individualized. In greenstick fractures of the maxilla with only slight malocclusion of the teeth, for example, immobilization by open reduction or extraoral appliances may not be necessary. Motion of the lower jaw against the upper will generally shift the teeth into occlusion.

Diagnosis.—In acute injuries of the face, the surgeon should have no difficulty in recognizing gross fractures of the facial bones, even without roentgenograms. Although roentgenograms afford valuable information and should be made in all cases as soon as the condition of the patient permits, as a rule, an accurate diagnosis may be made by careful inspection and palpation. Examination by palpation should be

ported by the immobilized large fragment. Following wiring fixation of the infraorbital ridge, intra-antral packing with gauze or other substance is unnecessary.

Should the maxilla be separated in the midline, the teeth on the fractured side are fixed to those of the sound side. In many cases a simple loop of wire is sufficient, though in more complicated cases, with loss of the teeth, an arch band may be required (Fig. 3).

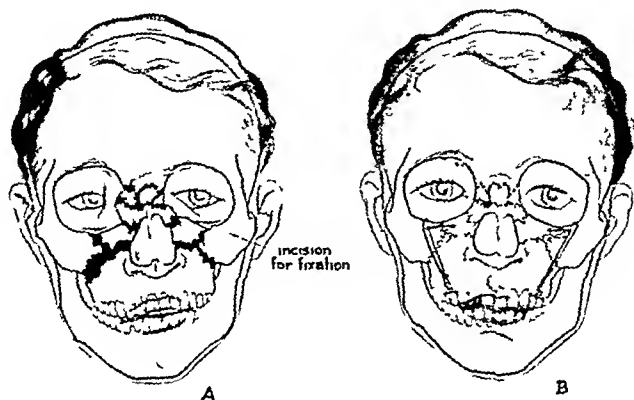


Fig. 2—A, Complete bilateral fracture of maxilla with comminuted fractures of nasal bones and infraorbital ridges. B, Maxilla held in position by wires from the malar bones to the upper teeth, lower fragments of infraorbital ridges immobilized by separate wiring, fixation not necessary for smaller fragments.

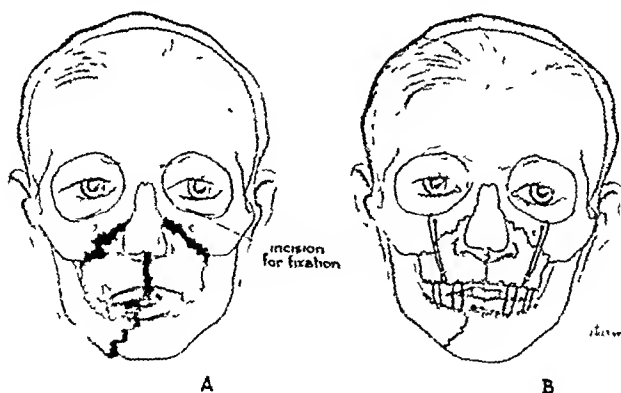


Fig. 3—A, Complete bilateral fracture of maxilla with separation in midline, associated compound fracture of the mandible at the symphysis. B, Metal arch bands attached to upper and lower teeth, fractures of maxilla reduced and held in normal position with wires from infraorbital ridges to upper arch bands on both sides, upper and lower teeth fixed in occlusion with orthodontic rubber bands.

For reduction and immobilization of fractures of the maxilla with associated fractures of the zygoma or malar process (Fig. 4), an incision is made over the ridge of the frontal bone lateral to the supra-

In a simple bilateral fracture of the maxilla (Fig. 1), a small incision is made over the infraorbital ridge on either side. A hole of sufficient size to accommodate a No. 25 or 26 stainless steel wire is bored through the infraorbital ridge. The wire is then threaded through the opening, looped over the ridge, and both ends are passed together along the anterior wall of the antrum into the upper sulcus over the second molar teeth, where they are caught with a hemostat. One is surprised at the ease with which the wires are directed to the desired point of exit without the use of a guide. The fractured bone is then elevated to its normal position and the wires are drawn taut and fixed to one or more of the teeth. The use of the loop around the infraorbital ridge is much more simple than tying the wire and its subsequent removal is easily accomplished.

If the patient is edentulous, the wires may be attached to the false plate, provided it is intact; otherwise, dental wax may be molded around the alveolar ridge and over the hard palate, the wires drawn across the palate and tied in the midline, and the ends imbedded in the wax.

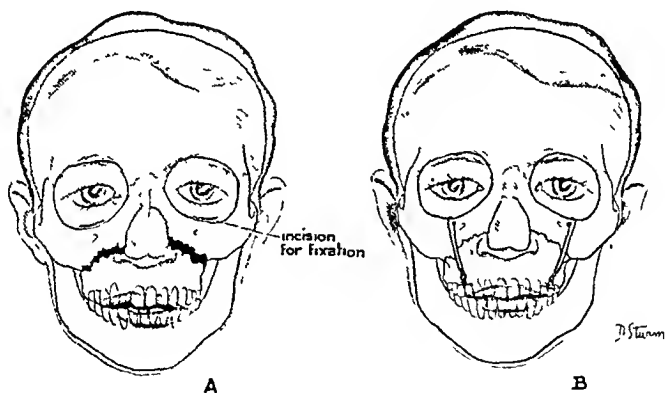


Fig. 1.—A, Complete bilateral horizontal fracture of maxilla. B, maxilla elevated and maintained in normal position with wires extending from the infraorbital ridges to the upper teeth.

Once the wires enter the contaminated field of the mouth, they should not be drawn upward through the soft tissues. If removal is necessary, the loop should be cut and the wires withdrawn from below.

In fractures of the maxilla associated with comminuted fractures of the infraorbital ridge (Fig. 2), it is sometimes necessary to immobilize the major fragment of the ridge to the outer half. This may be done through the same soft tissue incision. An additional hole is drilled through the medial fragment and a small loop of wire is inserted through the two holes and tied. The smaller fragments, after restoration to their normal position, will usually remain in place, being sup-

teeth, exerting an upward and outward pull on the malar bone, holding it up in normal position. Should there be any question as to the adequacy of fixation, one should not hesitate to drill another hole in the malar bone just below the zygomatic-frontal suture line and, with a small loop of wire, fix the malar bone to the zygomatic process of the frontal bone (Fig. 5, B_2).

In these cases, the malar bone and zygomatic process may be elevated by several other methods. By such methods, however, the malar bone, if completely detached, may subsequently be displaced by the strong pull of the masseter muscle. With the procedure described, the bones may easily be restored to their normal positions and the malar bone firmly fixed to the frontal bone by wiring, through the one incision. Associated fracture of the zygomatic arch, after reduction, does not require fixation, since it has adequate support from the underlying temporal muscle.

Following reduction and immobilization of fractures of the maxilla and other facial bones, associated fractures of the nasal bones are reduced and maintained in position by a nasal splint, according to the routine method of treating such fractures when encountered alone.

In bilateral fractures of the facial bones, the foregoing procedures are carried out, as indicated, on both sides. In bilateral horizontal fractures of the maxilla with separation in the midline (Fig. 3), the two halves are drawn together and immobilized with arch bands or wires. This should precede open reduction and fixation of the maxilla to the upper unfractured bones. If the mandible is not fractured, fixation of the upper to the lower jaw is unnecessary.

Oral Hygiene.—This is of the utmost importance. The mouth should be thoroughly irrigated every hour until the infectious stage has passed, and thereafter three or four times daily. Normal saline, boric acid, or any mild antiseptic solution may be used for the irrigations, though ordinary tap water suffices. Sterile solutions are neither practicable nor necessary. Unless quite sick, the patient may himself carry out the procedure. The equipment consists merely of a large douche can or intravenous flask and three feet of rubber tubing to which a hard rubber or metal irrigating tip is attached. The can is placed at least two feet above the patient's head, so that the force of the stream may be ample to insure adequate cleansing. In addition to this measure, the patient should be encouraged to brush his teeth with a small brush when possible.

The wires are allowed to remain in place for three to nine weeks, depending upon the location and type of the fracture. One may feel free to leave them undisturbed as long as necessary, since they cause little or no discomfort, as in the case when an extraoral appliance is used.

orbital rim, just above the zygomatic-frontal suture line. With an elevator, the periosteum is separated from the frontal bone and a small hole is drilled through the ridge. A wire is threaded through the opening, looped over the ridge, and the two ends are passed beneath the

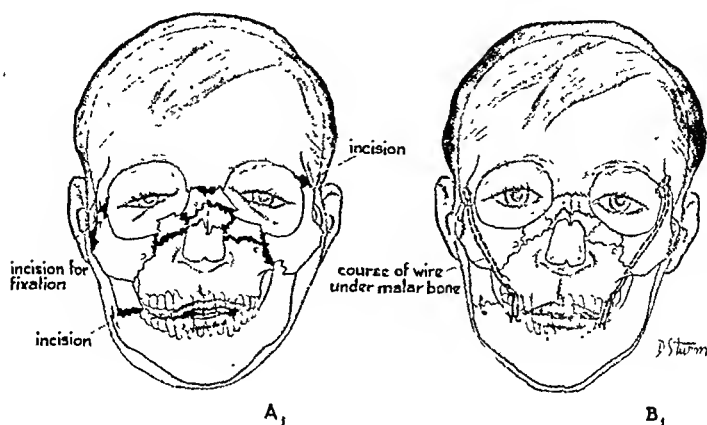


Fig. 4 (Case 1).—*A*₁, Complete bilateral fracture of maxilla, comminuted fracture of infraorbital ridges, and nasal wings, fracture of both malar bones; fracture of right mandible just above angle of jaw. *B*₁, Fracture of right malar bone reduced and wire passed from frontal bone behind body of malar bone and attached to upper teeth, fixing the maxilla and malar bones on this side. Same procedure repeated on left, and, in addition, malar wired separately to frontal bone because of gross displacement; fracture of right angle of mandible fixed by open reduction and wiring, upper and lower teeth wired in occlusion.

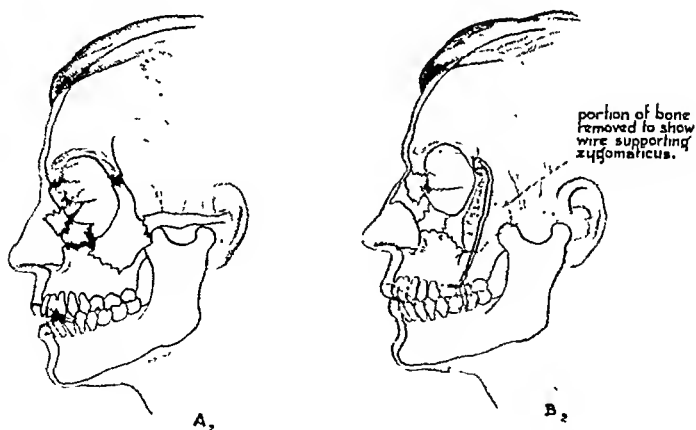


Fig. 5 (Case 1).—*A*₂, Lateral view, left side, showing fractures of the facial bones; *B*₂, lateral view, showing course of wire from the frontal bone to the upper teeth, supporting the malar bone in normal outward and upward position.

temporal surface of the malar bone, making their exit in the upper sulcus in the region of the first or second molar. The displaced bones are elevated to their proper positions and the wires are tied to the

After healing is complete, the wire is severed through a small spear-point incision over the loop and removed through the mouth, in order to avoid contamination of the soft tissues above.

Nature is kind in the treatment of these facial injuries, in that the blood supply of the tissues is abundant and healing takes place quickly. The scar over the infraorbital ridge, being horizontal, is almost invisible, while that over the supraorbital ridge is at the edge of the eyebrow and consequently is also inconspicuous.

In only one case treated by the above method has infection developed. This was a bilateral fracture of the maxilla with fractures of both zygomas and of the nasal bones. Paradoxically, it was the first case in which we ever used sulfanilamide locally. The drug was placed in the wound on only one side, and this was the wound which became infected. The wires were not disturbed, as the infection subsided following incision and drainage and treatment with hot compresses. There was no infection in the wound of the opposite side wherein sulfanilamide was not used.

The following cases illustrate the application of this procedure in the various types of fractures of the facial bones.

CASE 1.—W. W., a white male, aged 52 years, was lying on the floor, working on the rear axle of a car from which the wheels had been removed, when the jacks slipped and the axle fell across his face. He was admitted to the hospital four hours later, suffering acutely and in a state of mild shock. Pantopon was given and the routine treatment for shock, including glucose intravenously, was carried out.

On inspection, all the soft tissues of the face were grossly swollen, the eyelids being almost completely closed from the edema. The middle third of the face was elongated from displacement of the maxilla inferiorly and posteriorly, the orbital rim was elongated vertically from a downward displacement of the infraorbital ridges, there was a comminuted fracture of the nasal bones, and the malar bones were depressed. On palpation, it was apparent that all the facial bones were crushed. In addition, there was a fracture of the mandible just above the angle on the right, with anterior and lateral displacement of the posterior fragment.

Almost immediately following the emergency treatment, the patient had a severe rigor, followed by a temperature of 104°F. , and it was felt unwise to manipulate the fractures at this time. His fever subsided under treatment with sulfanilamide and two days later reduction and immobilization were carried out under local anesthesia.

The left malar bone was widely displaced, necessitating separate wiring to the zygomatic process of the adjacent frontal bone. Small holes were then drilled in the frontal bone lateral to the orbital region just above the zygomatic frontal suture line on both sides, a No. 25 stainless steel wire was threaded through the opening, and the two ends of the wire were carried downward behind the malar bone and under the soft structures of the cheek, into the upper sulcus of the mouth in the region of the first and second molars. After elevation of the zygomatic arches and malar bone, the soft tissue wounds were closed. Dyclet wires were next placed around the upper and lower molar teeth on both sides. The maxilla was then restored to its normal position and the wires from above were drawn taut and tied so those about the teeth of the lower jaw. In this manner the teeth were held in occlusion and, at the same time, the fractured bones were maintained

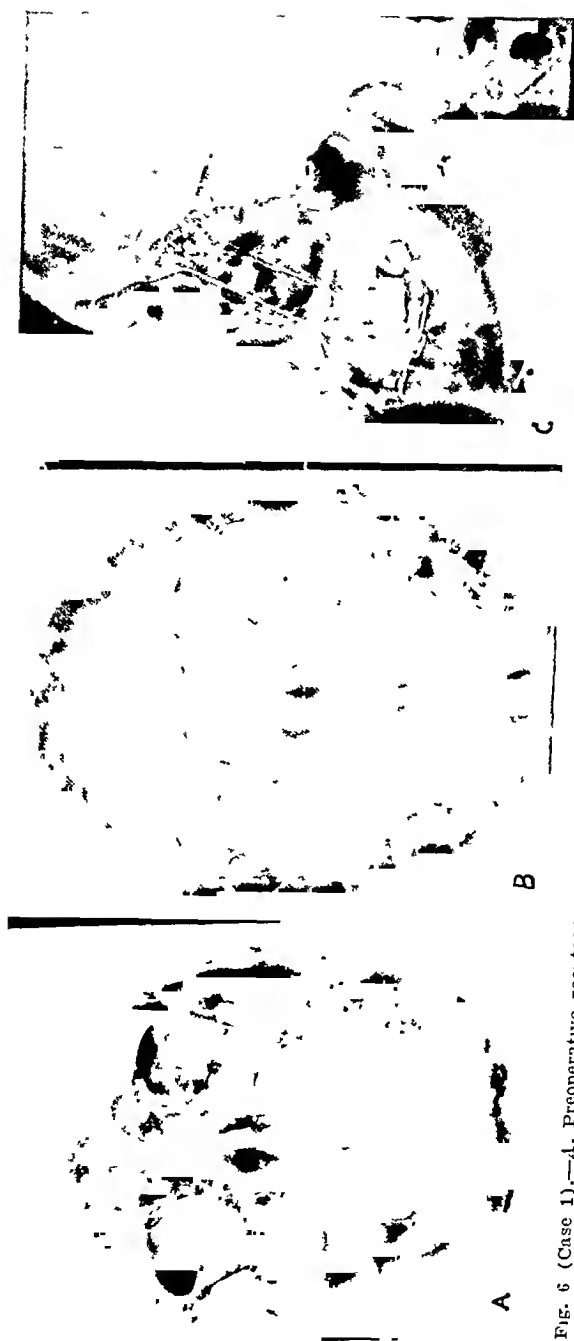


FIG. 6 (Case 1).—A, Preoperative roentgenogram, arrows designating fractures; B and C, roentgenograms after open reduction and fixation, points of wiring designated by arrows

in proper position. The anterior wall of the antrum was elevated with a male urethral sound inserted through the nares, the nasal bones were replaced, the passages packed with vaseline gauze, and an external nasal splint was applied.

Postoperative roentgenograms revealed the maxilla and other facial bones in good position. The displacement at the right angle of the mandible, however, was still apparent. Since it was impossible to reduce and maintain this fracture in normal position by manipulation, an incision 2 cm. long was made over the angle and the bones were apposed and fixed with a No. 25 stainless steel wire.

During the first week, oral irrigations were carried out hourly, supplemented by the use of oral pentacresol at frequent intervals. The patient had a slight temperature for several days, though this gradually subsided under treatment with sulfanilamide. He improved rapidly thereafter and was able to leave the hospital two weeks following his admission. The wires around the facial bones were removed in the office eight weeks postoperatively. Because of the fracture of the mandible, it was necessary to maintain fixation of the lower to the upper jaw for a longer period. The patient now has full motion in the lower jaw, both vertically and laterally, the teeth are in good occlusion, and the contour of the face is normal.

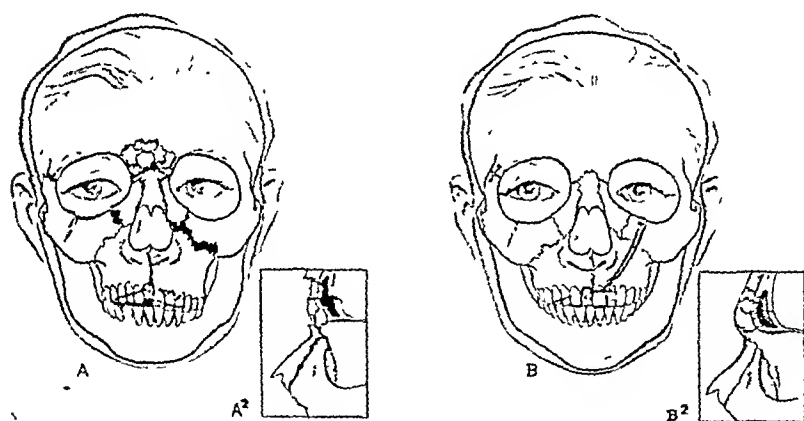


Fig 8 (Case 2).—A, Bilateral fracture of the maxilla, greenstick fracture of the right half, without displacement, complete bony detachment of the left half of the maxilla with downward displacement of the right malar bone, crushing fracture of the nasal bones and infraorbital ridges, depressed fracture of the anterior and posterior walls of the frontal sinus, fracture of the cribriform plate.

B, After reduction of fractures, the points of wiring fixation at the right zygomatico-frontal suture line and the left infraorbital ridge.

A2, Lateral view showing fractures of the frontal sinus region. B2, postoperative lateral view.

CASE 2.—H. A. was a white male, aged 33 years. He was a passenger on the front seat of a car which was driven into a telephone pole, causing the mid portion of his face to strike the instrument board. He was admitted to the hospital an hour later and immediately given routine treatment for shock.

There was a laceration two inches long through the periosteum of the forehead; multiple lacerations about the right eye; a deep stab wound over the upper part of the nose and frontal sinus region, extending into the frontal sinus and nasal cavity; lacerations of the right ala; and an irregular through and through laceration of the upper lip. The middle part of the face was depressed and elongated. The right upper central and lateral incisors had been knocked out, and the remaining upper, as well as the lower central incisors were loose.

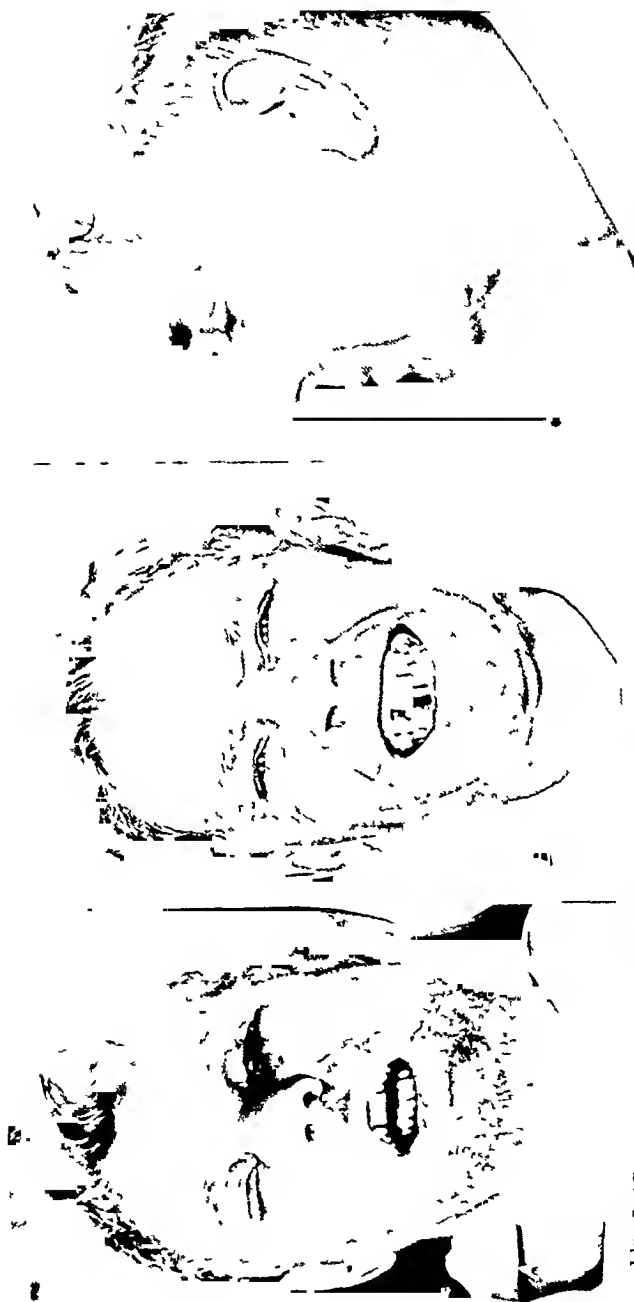


Fig. 7 (Case 1) —A, Preoperative photograph two days after injury the displacement of the facial bones is obscured by the swelling of the overlying soft structures. Due to the downward displacement of the maxilla the patient was unable to bring teeth of the lower jaw in occlusion with the upper jaw B, and C, Two months postoperative, showing teeth in occlusion and normal facial contour

in proper position. The anterior wall of the antrum was elevated with a male urethral sound inserted through the nares, the nasal bones were replaced, the passages packed with vaseline gauze, and an external nasal splint was applied.

Postoperative roentgenograms revealed the maxilla and other facial bones in good position. The displacement at the right angle of the mandible, however, was still apparent. Since it was impossible to reduce and maintain this fracture in normal position by manipulation, an incision 2 cm. long was made over the angle and the bones were apposed and fixed with a No. 25 stainless steel wire.

During the first week, oral irrigations were carried out hourly, supplemented by the use of oral pentacresol at frequent intervals. The patient had a slight temperature for several days, though this gradually subsided under treatment with sulfanilamide. He improved rapidly thereafter and was able to leave the hospital two weeks following his admission. The wires around the facial bones were removed in the office eight weeks postoperatively. Because of the fracture of the mandible, it was necessary to maintain fixation of the lower to the upper jaw for a longer period. The patient now has full motion in the lower jaw, both vertically and laterally, the teeth are in good occlusion, and the contour of the face is normal.

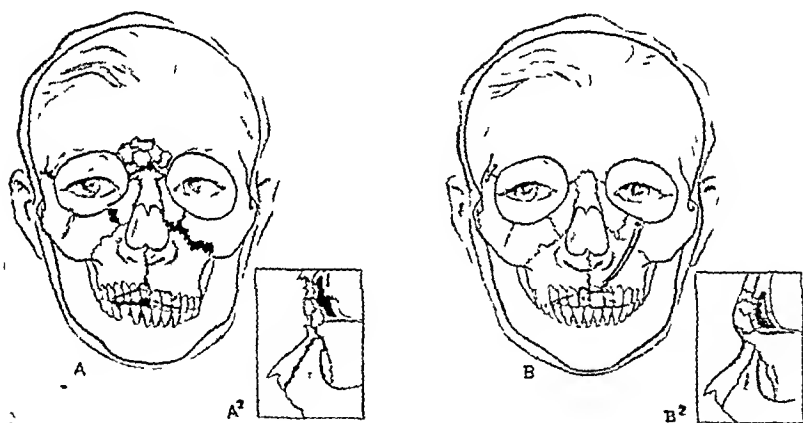


FIG 8 (Case 2) — 4. Bilateral fracture of the maxilla, greenstick fracture of the right half, without displacement, complete bony detachment of the left half of the maxilla with downward displacement of the right malar bone, crushing fracture of the nasal bones and infraorbital ridges, depressed fracture of the anterior and posterior walls of the frontal sinus, fracture of the cribriform plate.

B. After reduction of fractures, the points of wiring fixation at the right zygomatico-frontal suture line and the left infraorbital ridge.

A². Lateral view showing fractures of the frontal sinus region. B². post-operative lateral view.

CASE 2 — II. A. was a white male, aged 33 years. He was a passenger on the front seat of a car which was driven into a telephone pole, causing the mud portion of his face to strike the instrument board. He was admitted to the hospital an hour later and immediately given routine treatment for shock.

There was a laceration two inches long through the periosteum of the forehead; multiple lacerations about the right eye; a deep stab wound over the upper part of the nose and frontal sinus region, extending into the frontal sinus and nasal cavity; lacerations of the right ala; and an irregular through and through laceration of the upper lip. The middle part of the face was depressed and elongated. The right upper central and lateral incisors had been knocked out, and the remaining upper, as well as the lower central incisors were loose.

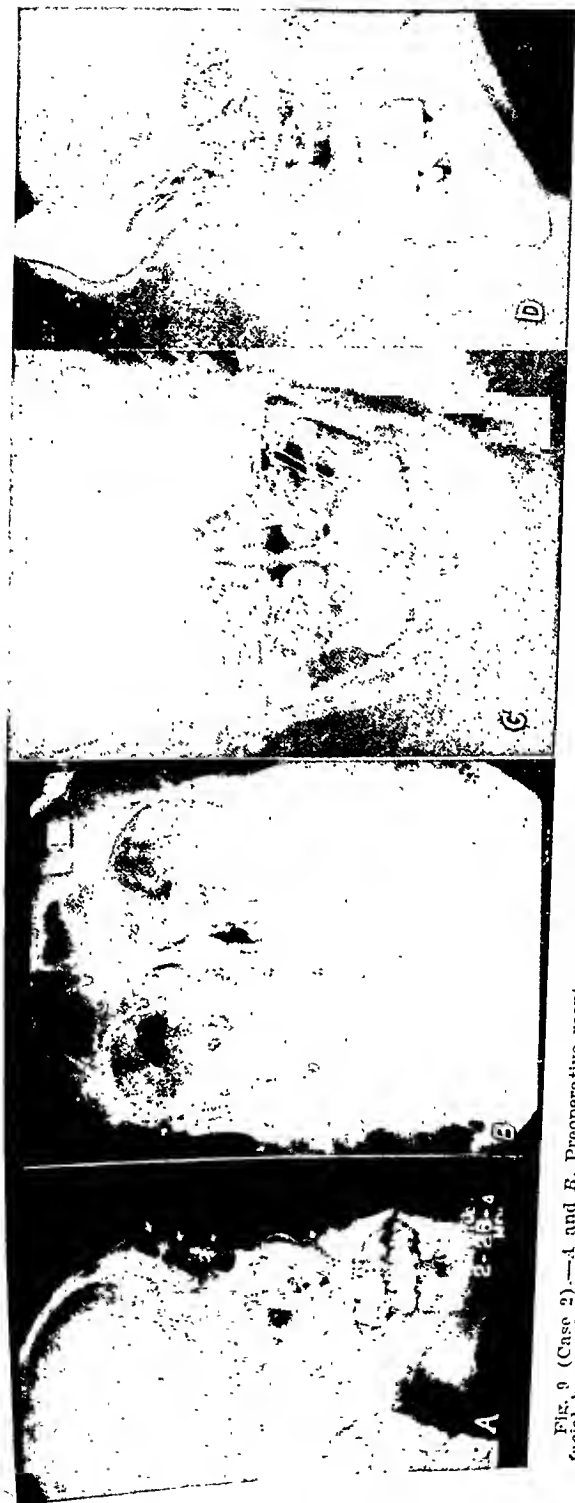


Fig. 9 (Case 2).—A and B, Preoperative roentgenograms; arrows designate fractures. C, Immediate postoperative roentgenogram showing facial bones in satisfactory position. D, Postoperative roentgenogram one year later; the wire at the right frontozygomatic suture line still in place, facial bones in satisfactory position.

Examination revealed a compound crushing fracture of the nasal bones extending into the frontal sinus; the anterior wall of the frontal sinus was depressed and in contact with the posterior wall, and there was an opening in the posterior



Fig. 10 (Case 2).—A, Photograph immediately after injury showing multiple lacerations and distortion of facial features; downward displacement of the right eye. B and C, Postoperative photograph one year later showing perfect occlusion of the teeth with satisfactory restoration of normal facial contour.

plate through which a small amount of brain tissue protruded. All the bony structures of this region were movable, including the cribriform plate. In addition, the infraorbital regions were crushed inward, there was a greenstick fracture

of the right maxilla without displacement, a fracture of the left half with gross downward and backward displacement, complete detachment of the right malar bone, and a depressed fracture of the zygomatic arch.

The skin about the wounds was thoroughly cleansed, local anesthetic given, and the wounds copiously irrigated with warm saline solution. Through one of the soft tissue wounds at the outer margin of the supraorbital ridge on the right, the fracture in the frontozygomatic region was exposed and with a heavy metal elevator and external manipulation, the malar bone and zygomatic arch were restored to normal position. The malar bone was anchored to the zygomatic process of the frontal bone with small stainless steel wire and the incision was closed.

Before manipulation of the fractures about the nose and maxilla, the nasal mucosa was cocaineized and the maxillary region was anesthetized with nerve block and deep infiltration of novocain. Through a small incision over the left infraorbital ridge, a hole was then drilled in the unfractured portion of the left malar bone and a loop of wire threaded through the opening and passed down beneath the soft tissues of the cheek along the interior wall of the antrum, into the upper sulcus. The fracture of the maxilla was next reduced, the occlusion of the teeth tested by bringing the lower jaw into contact with the upper and the wire tied around the upper teeth on the left side, holding the maxilla up in proper position.

Because of the fracture of the cribriform plate, extreme care was exercised in reducing the fractures about the nose and frontal sinus region. The anterior wall of the frontal sinus was elevated and the sinus again copiously flushed with normal saline solution. Since there was a large fracture opening from the frontal sinus to the nasal cavity, the overlying soft tissue wound was closed without external drainage.

After replacing the bony cartilaginous nasal septum in the midline, a small stainless steel wire was threaded through and through the nose over a lead plate on each side. With a trocar antial windows were then made under the inferior turbinates. In order to allow free drainage, packing of the nasal passages was omitted. The patient left the operating room in fairly good condition, though the prognosis was regarded as poor.

An examination by a neurosurgeon revealed nothing of particular significance except the presence of blood from the middle ear in the external auditory canal on the left. Only conservative treatment was therefore advised.

The patient was given 15 gr. of sulfanilamide every four hours and fluids were limited. His temperature reached its highest of $102\frac{1}{4}^{\circ}$ F. on the first postoperative day, and thereafter gradually subsided, reaching normal on the fifth day. The nasal splints were removed at the end of the week and he left the hospital three days later. His subsequent course was smooth, his only complaints being a double vision and vertigo. The fixation wire of the maxilla was removed in the office nine weeks after insertion.

It has now been two years since the injury and the patient has been working regularly for the past year and one half. His facial contour is normal, occlusion of the teeth is perfect, the nasal passages are unobstructed, his hearing is not appreciably impaired, and he no longer has double vision. On turning his head quickly from side to side, he has a transient vertigo as a result of the injury to the left semicircular canal, but otherwise has no noticeable difficulty from the injury.

CASE 3—T. S., a colored male, had been struck in the face by a train one hour before his admission to the hospital. In addition to multiple small lacerations about the face, he had a complete laceration of the upper lip in the midline, and a traumatic cleft extending through the alveolar ridge, the hard palate, and the nasal cavity, into the left antrum. The lower lip and tissues over the mandible were also completely lacerated in the midline and the symphysis was widely sepa-

rated. The two upper central incisors and the left lateral incisor were loose, and the lower central incisors had been knocked out. There was also a fracture of the zygomatic process on the right.

Roentgenograms demonstrated a greenstick fracture of the right maxilla without gross displacement, complete displacement of the right malar bone downward and inward with a fracture of the right zygomatic arch, a complete fracture of the left maxilla with the bone attached only to the soft tissues, detachment of the nasal bones from the frontal process with displacement to the right and downward, a crushing fracture of both infraorbital ridges downward, a midline fracture of the alveolar process extending into the hard palate with separation of the two halves, and a fracture of the mandible through the symphysis with wide separation.

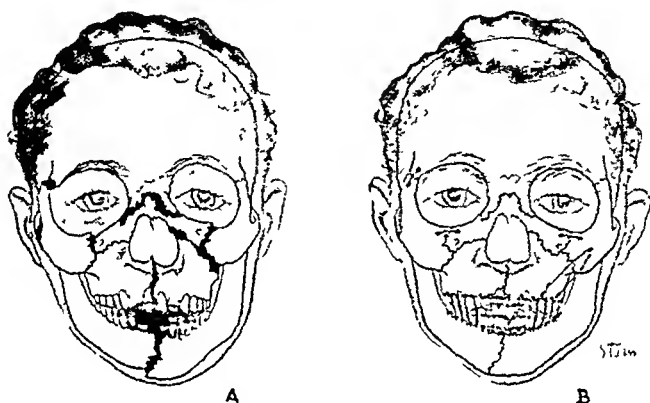


Fig. 11 (Case 3)—A, Bilateral fracture of maxilla, greenstick fracture of right half and complete detachment of left half, with separation in the midline, fracture of both infraorbital ridges, dislocation of right malar bone, and compound fracture of the mandible at the symphysis.

B, Arch bands wired to upper and lower teeth, left half of maxilla immobilized in proper position with wires extending from body of malar bone to left upper teeth, fracture parts of infraorbital ridges wired together and right malar bone held in position by wire through frontal bone. Fixation of greenstick fracture of right maxilla was unnecessary. Upper and lower teeth were maintained in occlusion with orthodontic rubber bands.

The soft tissue wounds were repaired immediately after the patient's admission to the hospital, but because of his poor condition, no attempt was made to treat the bony injuries. He ran a low grade temperature for a few days, during which time sulfathiazole was administered. As soon as his general and local condition permitted, arch bands were placed around the upper and lower teeth to bring together the midline fractures of the maxilla and mandible. The bones were then restored to their normal positions and the fractures of the infraorbital ridges were immobilized by separate wiring of the fractured parts to the malar bone on both sides. To maintain reduction of the left maxilla, a wire was looped through the maxillary process of the malar bone and the ends brought down and attached to the arch band about the teeth. The right malar bone was wired to the frontal bone at the suture line. Although there was slight motion of the right half of the maxilla, being a greenstick fracture without displacement, wiring fixation was unnecessary. The teeth of the upper and lower jaws were brought into occlusion and held in place with rubber bands between the arch wires.

The arch bands and wire supporting the left half of the maxilla were removed six weeks later. The patient had no postoperative complications, and the roentgenograms showed all the fractured parts in good position.

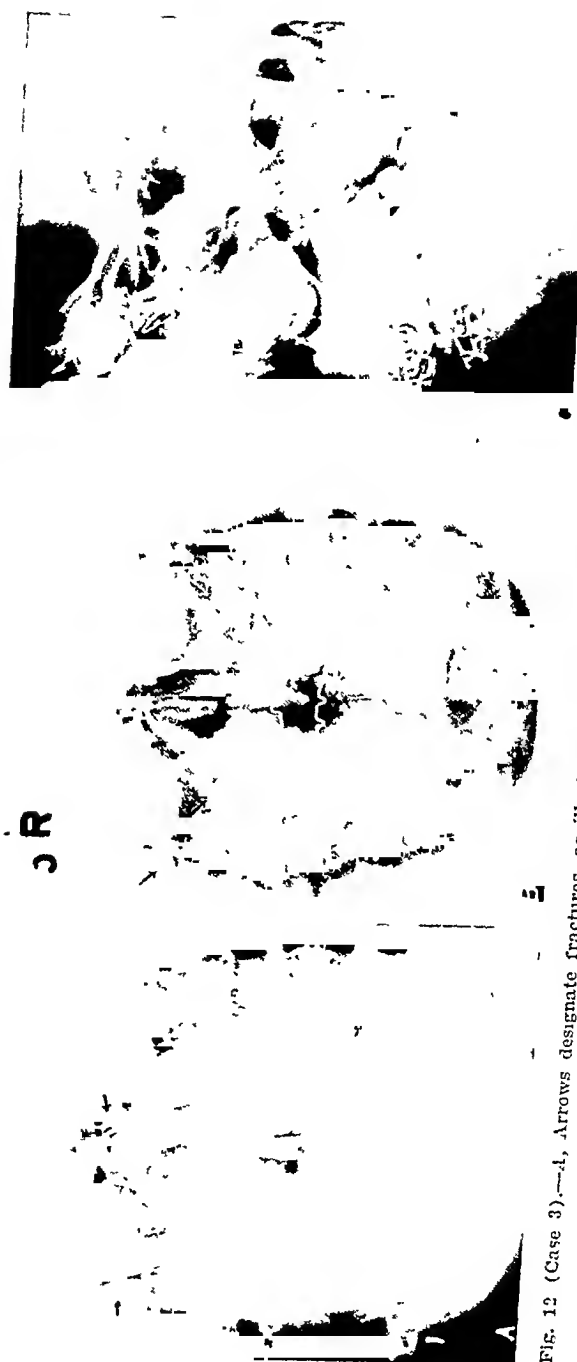


Fig. 12 (Case 3).—A, Arrows designate fractures, as illustrated in Fig. 11. B and C. Roentgenograms after open reduction and internal wiring; points of fixation designated by arrows.



Fig. 13 (Case 3) —A Preoperative picture one week after injury showing soft tissues still swollen, obscuring the deformity of the fracture and definite elongation of the middle one-third of the face. Patient unable to bring teeth in occlusion.
 B Postoperative photograph showing arch bands around upper and lower teeth held together with orthodontic rubber bands.
 C Postoperative photograph two months later showing normal facial contour. Scar of the upper lip may be improved by plastic repair.

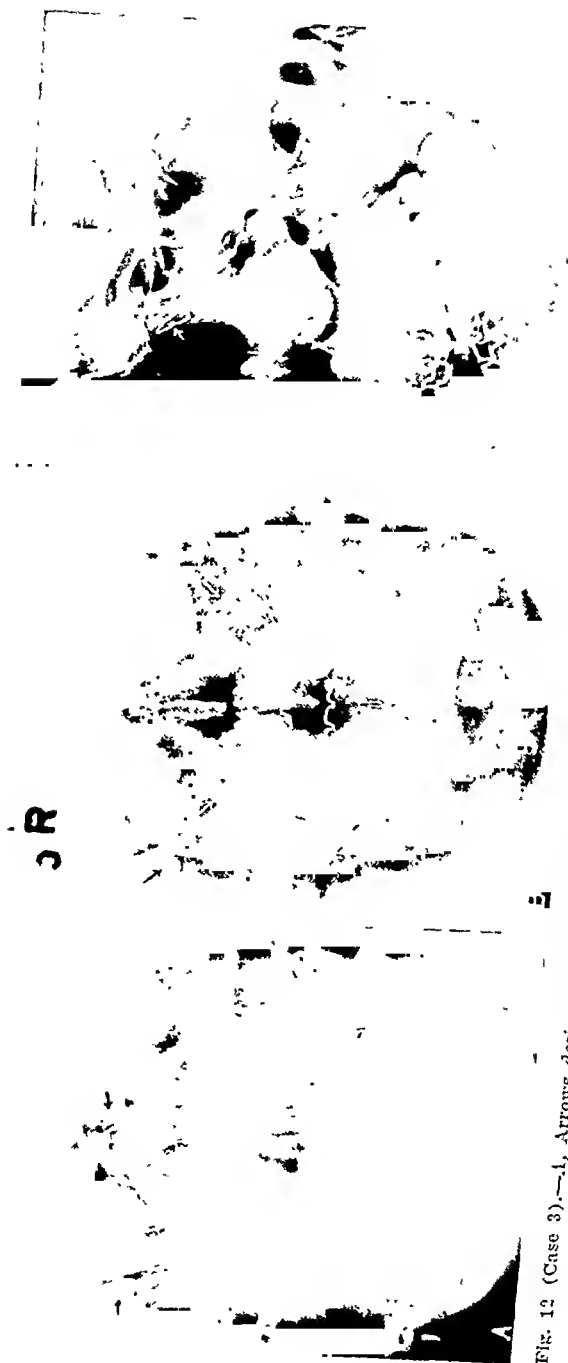


FIG. 12 (Case 3).—A, Arrows designate fractures, as illustrated in Fig. 11, B and C. Roentgenograms after open reduction and internal wiring; points of fixation designated by arrows.

THE BRONCHIAL FACTOR IN PULMONARY EMBOLISM

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IN PREVIOUS reports from this clinic, the reflex effects of pulmonary embolism on the heart¹ and on the pulmonary arterial tree² have been discussed. In this report we are presenting data concerning the behavior of the bronchial tree of the dog when pulmonary embolism is produced.

METHODS OF EXPERIMENTATION

Dogs weighing from 10 to 15 kg. were used. To visualize the bronchial tree, from 5 to 6 c.c. of iodochloral were injected with an 18 gauge needle directly into the trachea. The dogs were in a straight lateral position, with the head elevated from six to eight inches. The injection was made slowly, taking two and one-half minutes. After the injection had been completed, the animal's head was lowered to a horizontal position. For anesthesia, 0.3 c.c. of dial was injected per kilogram weight. The first film was taken five minutes after the injection was completed. The x-ray data were: the distance of the tube 29 inches, 30 Ma. with 70 to 75 kv. Exposure was 0.1 seconds. These factors were kept constant during the entire series.

The embolus was produced, as in our previous experiments from this laboratory,^{1, 2} by injecting a mixture of barium sulfate, iron perchloride and normal salt solution, equal parts, into the femoral vein. Throughout this series one-half cubic centimeter of this suspension was used.

RESULTS

Series I (Fig. 1A₁, B₁, C₁).—A bronchogram was obtained five minutes after intratracheal injection. The trachea and the larger bronchi are well visualized, including their finer branches. Immediately after the production of the embolus, the second exposure was made. The opaque material has been squeezed into the terminal radicals. The upper, middle, and lower main bronchi are invisible. The third film was taken eight minutes later showing little change, except more bullous dilations of the finer bronchi and patches of emphysema as a result of incomplete bronchial obstruction without infarction.³ In another experiment, in which only the upper branches were visualized, the same scattering of the iodochloral was observed, immediately, three minutes, and ten minutes after the embolism (Fig. 1A₂, B₂, C₂). In a third set the

¹Presented before the Central Society of Clinical Research, Chicago, Ill., Nov. 8, 1941.

SUMMARY

A simplified method of reduction and fixation of fractures of the maxilla and other faeial bones has been deseribed. For the approach, two small ineisions are used at the outer or inferior orbital ridge, on one or two sides depending upon whether the involvement is unilateral or bilateral. The proeedure requires a minimum amount of time and equipment, a small drill, pair of pliers, spool of small stainless steel wire, and a disseeting set.

Series II (Fig. 2).—After the visualization of the bronchi, the trachea of the animal was clamped with a six-inch, curved forceps causing marked dyspnea and cyanosis. Films were obtained at the height of respiratory distress, immediately after, and five minutes after release of the clamp.

Three such experiments were performed; none of them showed any change in the pattern of the bronchial tree. Cyanosis and dyspnea cannot be responsible for the bronchial spasm seen in the previous series.

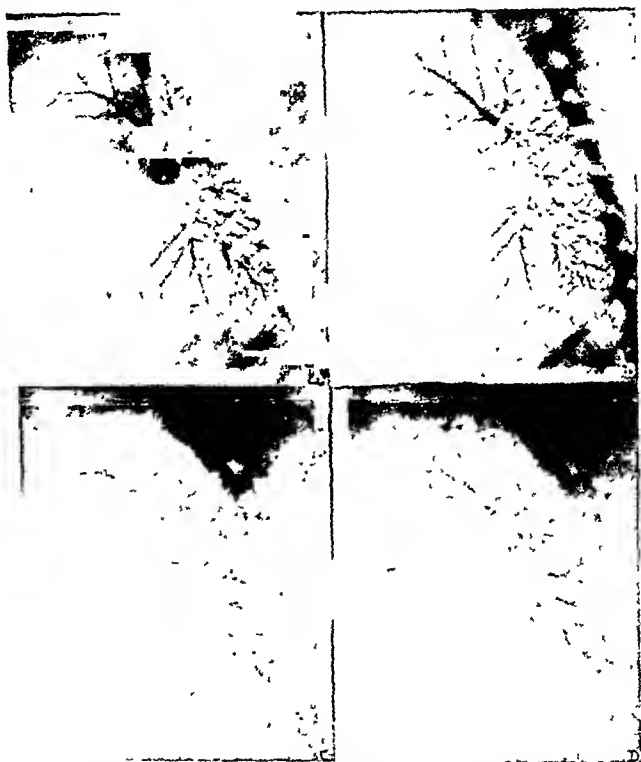


Fig. 2.—A, Control film; B, film was obtained at the height of respiratory distress after the trachea of the dog was clamped with a six-inch curved forceps, which caused marked dyspnea and cyanosis; C, immediately after the release of the clamp; D, five minutes after the release of the clamp.

Series III (Fig. 3).—After a control film, showing a good visualization of the upper bronchus, a bilateral vagal section was done in the neck and the second film obtained two minutes later. There seemed to be a slight dilatation of the main upper bronchus. The third film was obtained three minutes after the production of an embolus, showing no change in the caliber of the main bronchus. The last film was taken five minutes after the embolus, indicating no change in the bronchial tree.

Bilateral vagal section, performed in four experiments, prevented the appearance of a pattern seen in the first series and interpreted as bronchospasm.

typical pattern of the bronchial tree is shown again, before, three minutes, and ten minutes after embolism (Fig. 1A₃, B₃, C₃). Twelve experiments showed an identical pattern. They were accompanied by the classical dyspnea and cyanosis of pulmonary embolism.

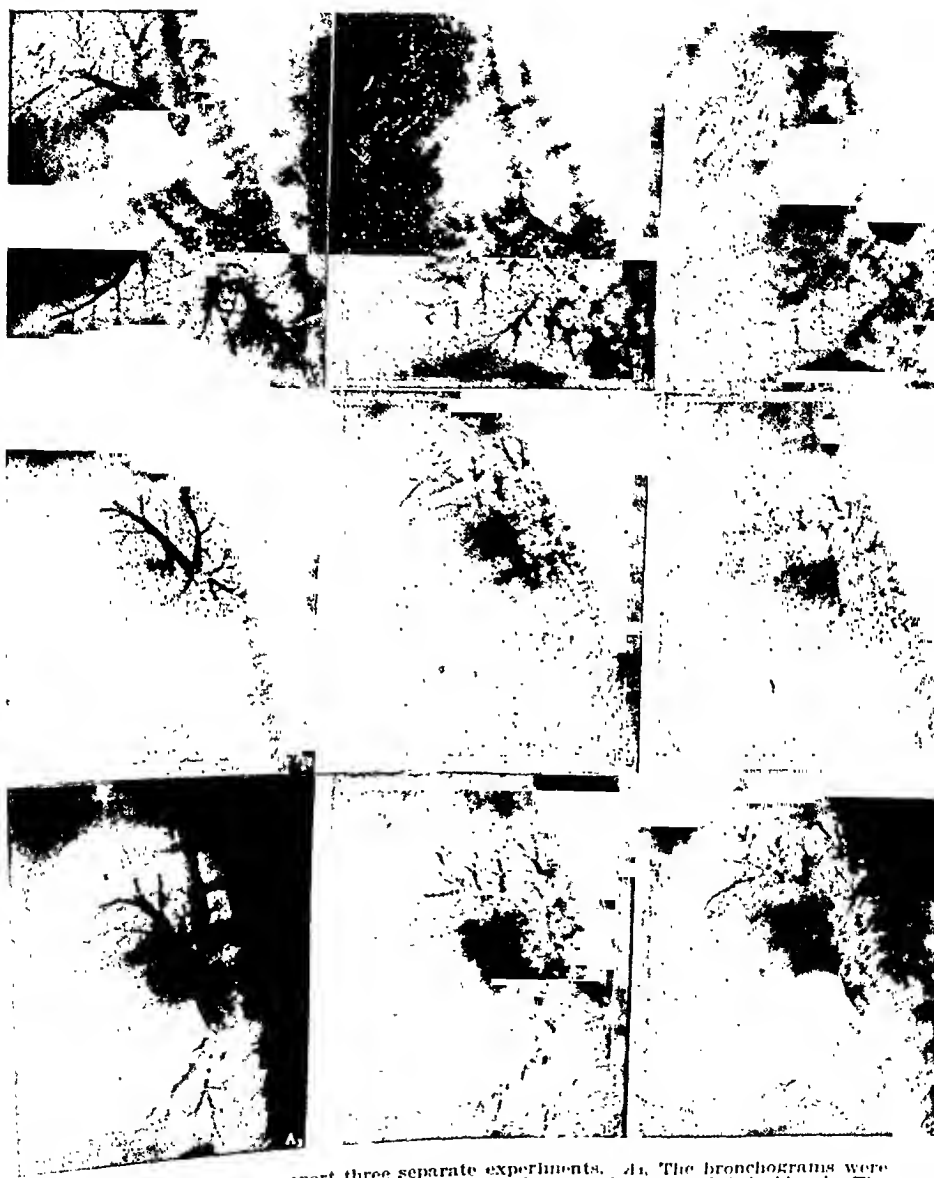


Fig. 1.—These films report three separate experiments. A₁. The bronchograms were obtained five minutes after an intratracheal injection of 5 cm. of Iodochloral. The trachea and the larger bronchi are well visualized. In A₂ the lower bronchi did not fill; in B the films were obtained immediately after the production of the embolus. The opaque material has been squeezed out of the larger bronchi into the terminal radicals. The upper, middle, and lower main bronchi are invisible. C. The third series of films were taken eight or ten minutes after the production of the embolus; the pattern has remained the same. Patches of emphysema are visible in these three films, which may well be the result of incomplete bronchial obstruction.

film, and a second one after atropine, $\frac{1}{75}$ gr., the embolism is produced. This did not affect the caliber of the bronchus, although some of the material must have trickled out. The fourth film was taken five minutes after the embolus and three seconds after the visualization of the right heart was undertaken by a method reported previously.² A comparison with the films shown in our previous report discloses the fact that this is a markedly enlarged right heart, a true cor pulmonale, which coexists with the absence of bronchial spasm prevented by $\frac{1}{35}$ gr. of atropine.

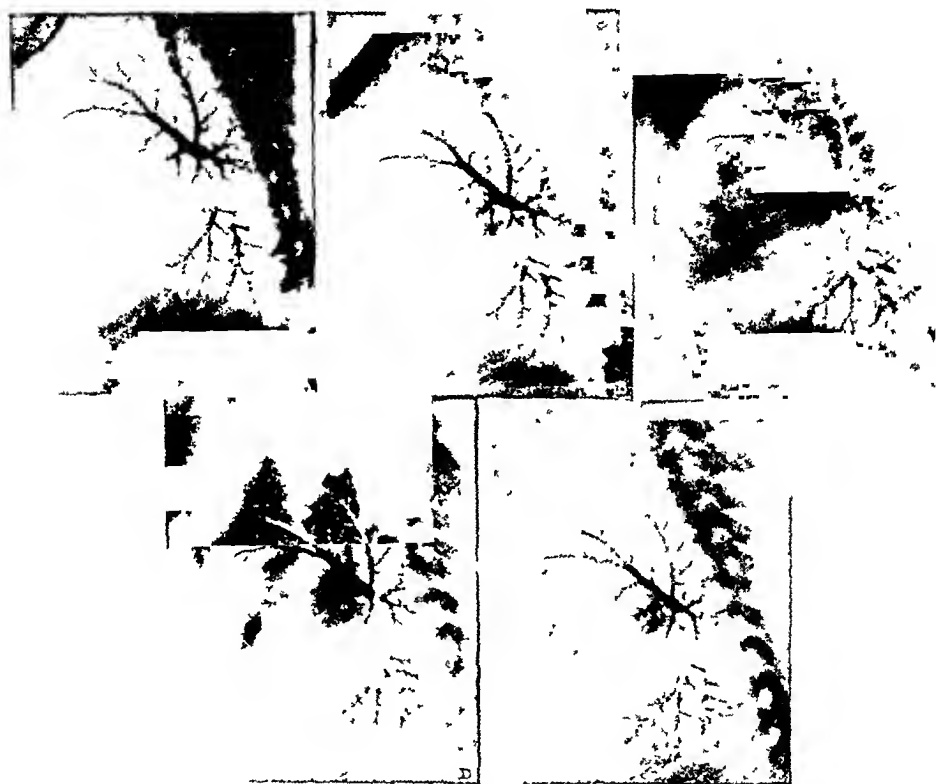


Fig 4—A, Control film showing very good bronchial tree. B, Film taken five minutes after intravenous injection of the embolus, there is no change in the pattern of the bronchi. C, E film taken five minutes after the production of the embolus with a maintained but scattered of the material in the lower lobes. D, Film showing no bronchial spasm. E, Film obtained five minutes after the production of the embolus, the pattern is fully maintained although the dog died immediately after this exposure.

Series VI—In a series of seven dogs, papaverine, $\frac{1}{2}$ gr., was given intravenously to test its protective action against bronchial spasm. Of the seven dogs, four obtained a result from this medication but the protection was never as complete as with atropine. In Fig. 7 a good bronchial pattern was obtained which was followed by a second film five minutes after the intravenous injection of $\frac{1}{2}$ gr. of papaverine. Immediately after the embolus the third film was obtained, which showed definite scat-

Series IV (Fig. 4).—After a control film showing visualization, $\frac{1}{75}$ gr. of atropine was injected intravenously and a film obtained five minutes later. There was no change in the pattern. Then the embolus was produced. The third film was taken immediately after the injection, showing slight scattering in the lower lobe. Two and five minutes later the pattern is still well maintained, although the dog died immediately after the last exposure.

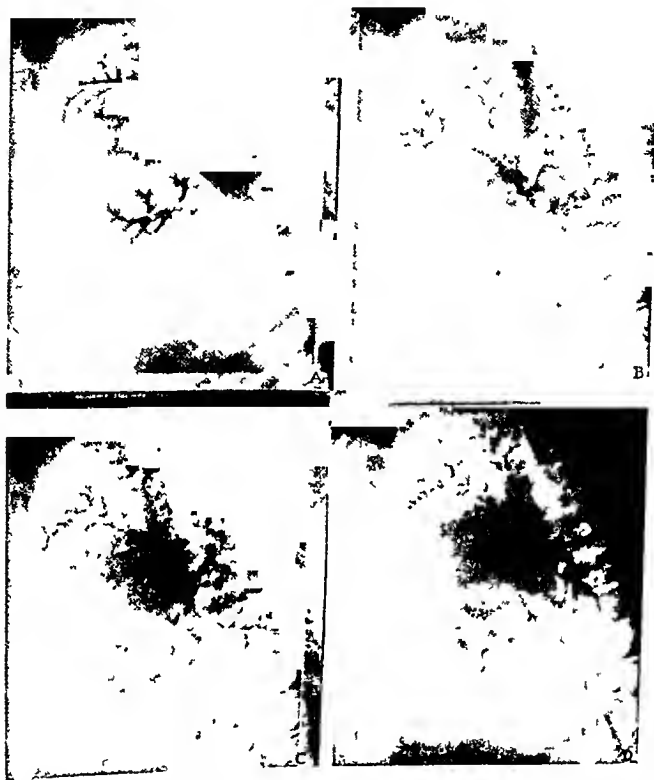


Fig 3—A, A control film was obtained showing good visualization of the upper bronchus. B, Film obtained two minutes after vagal section, the upper main bronchus seems to be more relaxed than in the control film, otherwise the pattern is the same. C, Was obtained three minutes after the production of the embolus showing no change in the caliber or pattern of the main bronchus. D, This film was obtained five minutes after the production of the embolus, the original pattern is still being maintained.

In a total of twelve experiments $\frac{1}{75}$ gr of atropine preserved the bronchial pattern in seven and failed to do so in five instances.

Series V.—In using $\frac{1}{35}$ gr. of atropine in a series of nine dogs, six of them obtained a complete protection from bronchial spasm. In Fig. 5, a control film was obtained, a second one five minutes after the atropine was injected, the third film immediately after the embolus was produced, and the last one three minutes later, at which time the animal died. There is no evidence of bronchial spasm in these films.

As further evidence that these dogs die of pulmonary embolism and yet exhibit no bronchial spasm, we show Fig. 6 in which, after a control

available for study. A clear-cut bronchial spasm was demonstrated after embolism in every instance; the bronchial pattern was distorted and the opaque substance scattered in all of them. Using this series of twelve dogs, in which bronchial spasm was obtained in 100 per cent as a control, the protecting or modifying methods gave the results shown in Table I.

While the series is small, the obtained percentages approximate closely the larger series obtained previously,¹ in which the death of the animal was prevented from embolism by employing vagal section, atropine, or papaverine. Possibly a higher dose of atropine, $\frac{1}{6}$ gr., might have resulted in a higher incidence of protection from spasm.

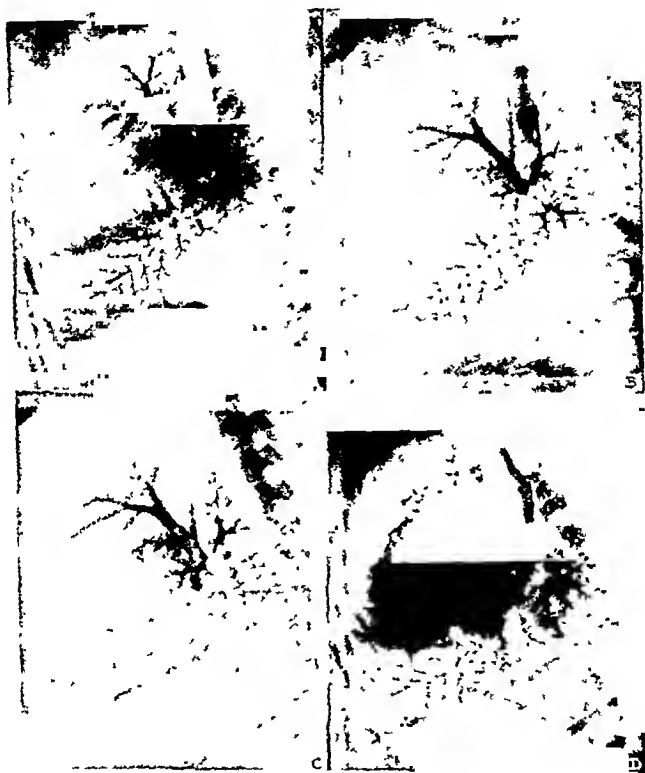


Fig 6—A, Control film B, Film obtained after the intravenous injection of atropine, $\frac{1}{2}$ gr C, Immediately after the production of the embolus which did not affect the caliber of the bronchus, although some of the opaque material must have trickled out D, Film obtained five minutes after the production of the embolus and three seconds after the visualization of the right heart this last film shows that a true cor pulmonale has been produced and yet bronchial spasm has been prevented by $\frac{1}{2}$ gr of atropine.

COMMENT

The production of pulmonary embolism followed by visualization of the bronchial tree reveals in each instance a disappearance of the visible pattern of the main bronchi. That this is due to bronchial spasm is shown by the experiments in which this change in pattern was inhibited.

tering although the pattern of the major bronchi was not lost as in the films obtained in the first series without medication. A film taken five minutes later shows a definitely improved pattern as if the papaverine had had a delayed action. The action is slower and, as will be discussed, of a different nature than that of atropine.



Fig. 5—A, The upper main bronchus is well visualized. B, Film obtained five minutes after the intravenous injection of $\frac{1}{2}$ gr. of atropine. C, This film was obtained immediately after the production of the embolus. D, Exposure made three minutes after the production of the embolus, at which time the animal died; there is no evidence of bronchial spasm in these films.

Series VII—In a series of nine dogs in which the prevention of bronchial spasm was attempted with a medication of atropine, $\frac{1}{75}$ gr., and papaverine, $\frac{1}{2}$ gr., only six obtained good protection. This has been shown in Fig. 8. The four films were taken before, five minutes after the drugs, immediately after the production of the embolus, and four minutes later in an agonal condition. The prevention of bronchial spasm was satisfactory. In Fig. 9, after a control film, the drugs were injected, the second film was taken immediately after the embolus, the third one five minutes later. There is no protection from spasm in these films.

SUMMARY OF EXPERIMENTS

In a total of sixty-three dogs, 316 exposures were made; some of these had to be discarded for technical reasons, so that fifty-three dogs were

have here another instance of reflex vagal impulses occurring during pulmonary embolism. We have discussed in a previous paper the possible sources of such reflexes.¹ They may originate from the hypertension in the pulmonary artery,⁴ from the powerful myelinated receptors of the bronchial musculature,⁵ from the congestion of the lung,⁶ and from pleural irritation.⁷ These reflexes have effects on the heart, on the pulmonary vascular bed, and on the bronchi, as shown in this report.

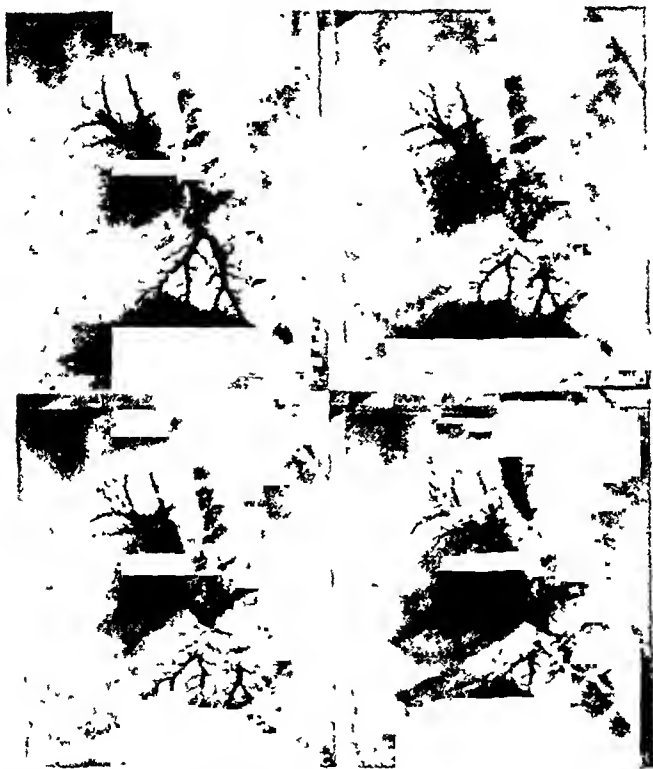


Fig. 8.—A, Control film. B, Film obtained five minutes after intravenous injection of atropine, $\frac{1}{32}$ gr., and papaverine, $\frac{1}{2}$ gr. C, Film obtained immediately after the production of the embolus showing some maintenance of the pattern. D, Film obtained four minutes after the production of the embolus with a well-maintained pattern, the pattern has

Hardly any attention has been given to this bronchial factor in the past. Singh⁸ reported the presence of bronchial spasm during air-embolism and recommended epinephrine for its relief. Neither atropin nor vagal section abolished the spasm in his experiments. Epinephrine in our previous experiments^{1, 2} exerted a deleterious effect on the animal subjected to pulmonary embolism. It is true that it stimulates the sympathetic bronchodilators and relaxes the bronchial tree, but it also raises the pressure in the pulmonary artery and precipitates pulmonary edema. Its clinical use in pulmonary embolism is inadvisable.

TABLE I

SUMMARY OF EXPERIMENT

NUMBER OF DOGS	NATURE OF TREATMENT	PERCENTAGE OF SPASM IN PER CENT
12	Control	0
12	Atropine, gr. $\frac{1}{100}$	58
9	Atropine, gr. $\frac{1}{50}$	67
7	Papaverine, gr. $\frac{1}{50}$	40
9	Atropine, gr. $\frac{1}{100}$ plus papaverine, gr. $\frac{1}{50}$	66
4	Bilateral vagal section	100
55		

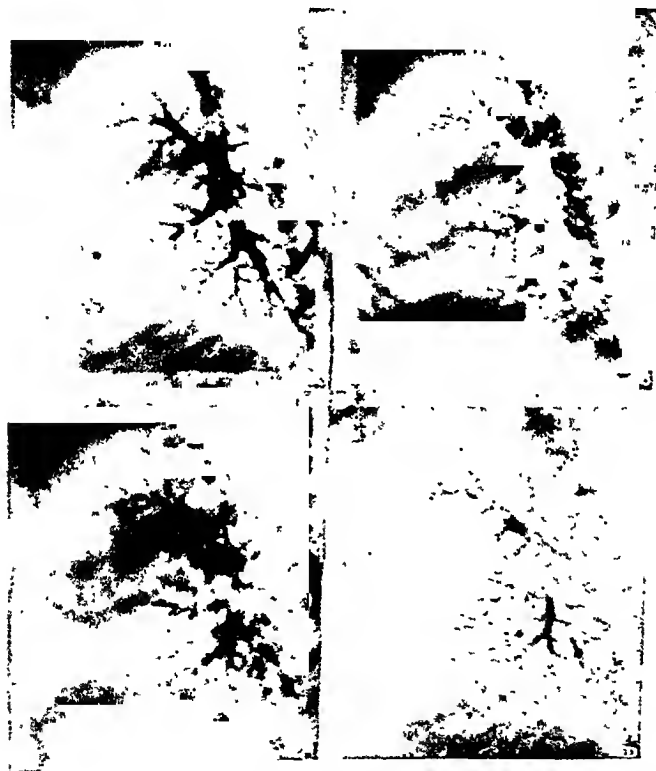


FIG. 7.—A. Control film showing a good bronchial pattern. B. Film obtained five minutes after the intravenous injection of $\frac{1}{100}$ gr. of papaverine; there is no obvious change in the pattern. C. Film obtained immediately after the production of the embolus; this film shows definite scattering, particularly in the lower lobe, although the pattern of the major bronchi has not been lost. D. Film taken five minutes after the production of the embolus showing a definitely improved pattern, as if the papaverine had begun to act; this series of films would indicate that the action of papaverine is more delayed than that of atropine.

either by bilateral vagal section or by $\frac{1}{100}$ gr. of atropine. The spasm is not due to hypernea or anoxemia, as mechanical obstruction to the trachea fails to produce the marked scattering of the opaque substance into the final radicals.

As vagal stimulation produces bronchial constriction and surgical or pharmacologic block of the vagus abolishes the bronchial spasm, we

have here another instance of reflex vagal impulses occurring during pulmonary embolism. We have discussed in a previous paper the possible sources of such reflexes¹ They may originate from the hypertension in the pulmonary artery,⁴ from the powerful myelinated receptors of the bronchial musculature,⁷ from the congestion of the lung,⁶ and from pleural irritation.⁷ These reflexes have effects on the heart, on the pulmonary vascular bed, and on the bronchi, as shown in this report.

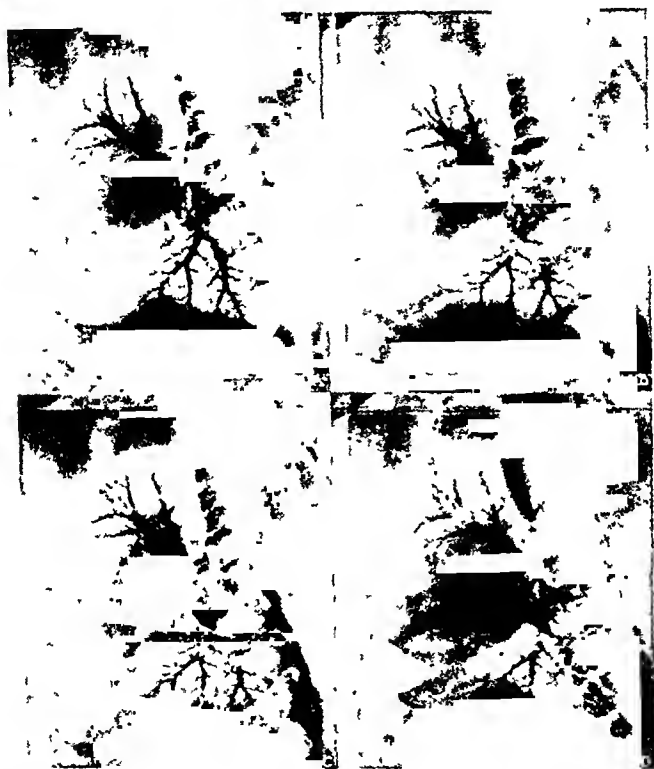


Fig. 8—A, Control film B, Film obtained five minutes after intravenous injection of atropine, $\frac{1}{75}$ gr., and papaverine, $\frac{1}{4}$ gr. C, Film obtained immediately after the production of the embolus showing some scattering but still a maintenance of the pattern D, Film obtained four minutes after the production of the embolus with a well-maintained pattern, the pattern has improved in this last film

Hardly any attention has been given to this bronchial factor in the past. Singh⁸ reported the presence of bronchial spasm during air-embolism and recommended epinephrine for its relief. Neither atropin nor vagal section abolished the spasm in his experiments. Epinephrine in our previous experiments^{1, 2} exerted a deleterious effect on the animal subjected to pulmonary embolism. It is true that it stimulates the sympathetic bronchodilators and relaxes the bronchial tree, but it also raises the pressure in the pulmonary artery and precipitates pulmonary edema. Its clinical use in pulmonary embolism is inadvisable.

Binet and Burstein⁹ studied bronchial spasm as a result of anaphylactic shock, histamine and acetyl choline injections, and pulmonary embolism. They used an intratracheal cannula during their experiments and obtained kymographic records, which are greatly influenced by respiratory movements. We repeated these experiments but felt that our present method of bronchography yielded a more definite and simple graphic record.

That papaverine relaxes bronchial musculature has been known ever since Pal's initial observations on this drug.¹¹ In our experiments its actions were slower and much less marked than that of atropin. Nevertheless, its use is highly important because of its effect on coronary flow and the pulmonary vascular bed.⁷ According to Linder and Katz¹² the drug inhibits ventricular fibrillation, which is frequently the immediate cause of death from pulmonary embolism.



Fig. 9—A, Control film. B, Five minutes after the intravenous injection of 1-2 gr. of atropine and $\frac{1}{2}$ gr. of papaverine, the embolus was produced immediately before this film was taken and shows a marked scattering of the material and, thus, no protection from spasm. C, Film obtained five minutes after the production of the embolus in which there is still a great deal of scattering, although some recovery of the original form of the bronchial tree. This group of films shows that the medication used has not been effective in preventing bronchial spasm.

CLINICAL APPLICATIONS

We have repeatedly stressed our belief that reflexes originating at the time of pulmonary embolism contribute to the causes of death and have suggested simple emergency measures for its control. Outside of oxygen, which is obviously helpful for cyanosis and dyspnea, intravenous injections of atropine ($\frac{1}{60}$ to $\frac{1}{75}$ gr.) and papaverine ($\frac{1}{2}$ gr.) were recommended.¹² The appearance of bronchial spasm, concomitant with pulmonary embolism, has been seemingly ignored in the past and can be inhibited, at least in the animal experiment, by atropin.

The bronchial asthma of pulmonary embolism explains the frequent finding of atelectatic areas in the x-ray films of patients suffering from pulmonary embolism. The vagal stimulus produces not only bronchial

constriction but also bronchial secretion. The bloody mucous plug in the bronchi seen at autopsies of patients dead from pulmonary embolism is the cause of atelectasis and patchy bronchopneumonias. Haight and Ransom¹³ have recently re-emphasized the prompt recognition and treatment of retained bronchial secretions following operations by posture, coughing, tracheobronchial suction, and bronchoscopy. They stress hypoventilation as the most important factor in the retention of bronchial mucus. Cutler¹⁴ for many years has held the embolic theory of postoperative lung reactions, feeling that small emboli may pass through the lymphatics of the diaphragm and cause pulmonary complications. Our present series of experiments suggest that some of these bronchial obstructions may be of reflex nature, either originating from pulmonary emboli or possibly from intra-abdominal sources of irritation. Thus, it has been sufficiently established that distention of the stomach¹⁵ or increased pressure in the biliary system¹⁶ produces vagal effects on the heart, which can be abolished by atropine. Experiments are contemplated in the future to see whether an effect on the bronchi can be produced by intra-abdominal manipulations.

The use of atropine in the presence of bronchial obstruction and hypersecretion may be objected to by many who feel that this drug increases the viscosity of the bronchial mucus and hinders evacuation. In the first few minutes and hours following pulmonary embolism, however, its administration dilates the bronchi and suppresses secretion. In a total of twenty-eight cases of pulmonary embolism observed at St. Luke's hospital, the atropine-papaverine mixture was administered in every instance. The drugs were given immediately after the recognition of the embolus and four to five days after, three times a day. No massive or patchy atelectasis was seen in this group, indicating that at least this medication does not increase bronchial obstruction to a harmful degree.

SUMMARY

The bronchial tree of the dog was visualized and the effect of pulmonary embolism on the pattern of the bronchial tree was studied. It was found that a powerful bronchoconstriction was produced during embolism, which could be abolished by bilateral vagal section and often by sufficient doses of atropin. Mechanical obstruction to the trachea failed to produce bronchial spasm. Papaverine failed to protect the bronchial tree from this reflex spasm in most instances. These experiments emphasize the existence of widespread autonomic reflexes which occur within the distribution of vagal fibers. The suppression of these reflexes decreases the morbidity and mortality from pulmonary embolism.

Our thanks are due to Miss Lillian Ryan, R.N. of the Neurocirculatory Clinic and Mr. Art Hesse for their valuable technical assistance.

REFERENCES

1. de Takáts, G., Boek, W. C., and Penn, G. K.: Pulmonary Embolism, *STREFFY* 6: 339, 1939.
2. Jesser, J. H., and de Takáts, G.: Visualization of the Pulmonary Artery During Its Embolic Obstruction, *Arch. Surg.* 42: 1034, 1941.
3. Westermarck, N.: On the Roentgen Diagnosis of Embolism, *Acta radiol.* 19: 357, 1938.
4. Schwiagh, H.: Der Lungenentlastungs Reflex, *Pflüger's Arch. f. d. ges. Physiol.* 236: 206, 1935.
5. Sunder-Plassmann, P.: Über nervöse Receptorenfelder in der Wand der intrapulmonalen Bronchien des Menschen und ihre klinische Bedeutung, insbesondere ihre Shockwirkung bei Lungenoperationen, *Deutsche Ztschr. f. Chir.* 210: 249, 1933.
6. Harrison, W. G., Jr., Calhoun, J. A., Marsh, J. P., and Harrison, T. R.: Congestive Heart Failure. XIX. Reflex Stimulation of Respiration as the Cause of Evening Dyspnea, *Arch. Int. Med.* 53: 721, 1931.
7. Cupps, J. A., and Lewis, D. D.: Observation Upon Certain Blood Pressure Lowering Reflexes That Arise From the Irritation of the Inflamed Pleura, *Am. J. M. Sc.* 134: 868, 1907.
8. Singh, I.: Certain Effects of Pulmonary Gas Embolism, *J. Physiol.* 87: 11, 1936.
9. Binet, L., and Burstein, M.: Recherches sur la motricité des bronches, *Presse méd.* 47: 217, 1939.
10. Pal, J.: Das Papaverin als Gefäßmittel und Anästheticum, *Deutsche med. Wchnschr.* 40: 164, 1914.
11. Linder, Erna, and Katz, L. N.: Papaverine Hydrochloride and Ventricular Fibrillation, *Am. J. Physiol.* 133: 155, 1941.
12. de Takáts, G., and Jesser, J. H.: Pulmonary Embolism; Suggestions for Its Diagnosis, Prevention and Management, *J. A. M. A.* 114: 1415, 1940.
13. Haight, L., and Ransom, H. K.: Observations on the Prevention and Treatment of Postoperative Atelectasis and Bronchopneumonia, *Ann. Surg.* 114: 243, 1941.
14. Cutler, E. C.: The Operative Efforts to Be Directed Toward the Prevention of Pulmonary Complications Through the Embolic Route, *Internat. Abstr. Surg.* 68: 340, 1939.
15. Gilbert, N. C., Penn, G. K., and LeRoy, G. V.: The Effect of Distention of Abdominal Viscera on the Coronary Blood Flow and on Angina Pectoris, *J. A. M. A.* 115: 1962, 1940.
16. Owen, S. E.: A Study of Viscero-cardiac Reflexes. 1. The Experimental Production of Cardiac Irregularities by Visceral Stimulation, *Am. Heart J.* 8: 496, 1933.

REGIONAL LYMPHATIC METASTASES OF CARCINOMA OF THE GASTROINTESTINAL TRACT*

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THE purpose of this paper is to compare the gross and microscopic characteristics of carcinoma of the gastrointestinal tract to the incidence of regional lymph node metastases. For a more detailed discussion of the anatomy of the lymphatics of the gastrointestinal tract and the location of the lymphatic metastases incident to carcinoma, the reader is referred to the previous communications upon this subject.¹⁻³

This study is based upon the dissection and examination of all the lymph nodes from 152 operative specimens of carcinoma of the gastrointestinal tract, including 53 gastric, 46 colonic, and 53 rectal specimens. The lymph nodes were dissected from each specimen after they had been visualized (Fig. 1) by clearing by the Gilehrst and David⁴ modification of the Spalteholz method. All nodes were examined microscopically and the results charted upon diagrammatic drawings, upon which every node was indicated (Figs. 2, 3, 4, and 5). The presence or absence of regional lymph node metastases was then correlated with (1) the age of the patient, (2) duration of symptoms, (3) gross type of neoplasm, (4) size, (5) circumferential extent (of colonic and rectal cases), (6) depth of infiltration, (7) microscopic type, and (8) the degree of cellular differentiation.

Regional lymph nodes which may be isolated thus go unnoticed by the usual method of dissection. Many large nodes were found to be inflammatory and many small impalpable nodes were found to contain metastatic carcinoma. Unless a lymph node was definitely replaced by carcinoma, it was impossible to determine without microscopic examination whether it was involved. These observations demonstrate clearly that operative procedures should not be minimized because of the absence of palpable lymph nodes.

As a result of this special method of investigation, 75.5 per cent of the gastric carcinomas, 60.87 per cent of the colonic carcinomas, and 64.2 per cent of the rectal carcinomas were found to have regional lymph node metastases. There were 30.2 nodes per specimen isolated in the gastric series in comparison to 52.07 nodes for the colonic series, and 67 nodes per specimen for the rectal group. The greater the number of nodes isolated in the individual groups, the higher the incidence of lymphatic metastases found. The comparative groups are shown in Table 1.

*This study was aided in part by a grant from the James and Elizabeth Inglis Fund for Surgery Research

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The carcinomas of the colon should have the most favorable prognosis of the entire group. They not only had the lowest incidence of regional lymph node metastases in our series, but they also had the largest number of cases in which only one lymph node was involved. Eleven of the colonic neoplasms were found to have only one positive node which was located close to the primary site in the majority of the cases. This was also true in 5 of the gastric cases and 6 of the rectal.

Not only did the gastric and rectal series have a higher incidence of lymphatic metastases, but they also had a higher incidence of microscopic infiltration into blood vessels in the absence of gross hematogenous metastases. There was an incidence of 15 per cent microscopic infiltration of blood vessels in both the gastric and rectal series, and only 10 per cent in the group of colonic carcinomas.

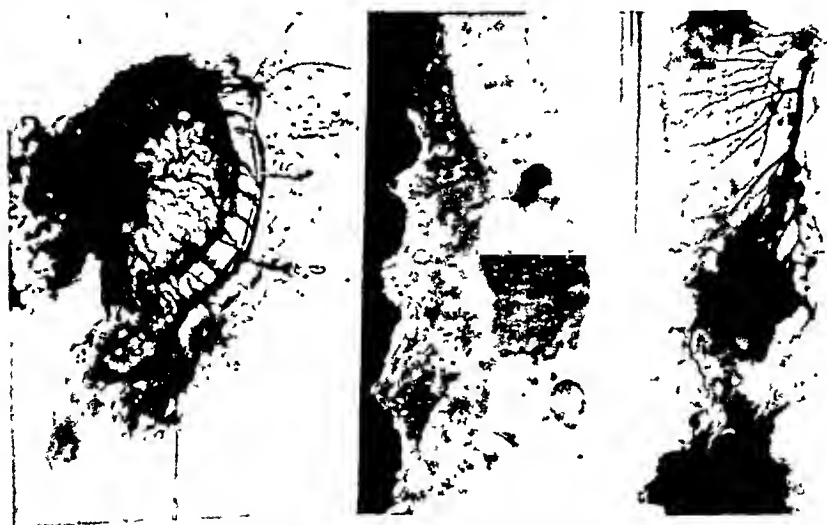


Fig. 1.—Photographs of the cleared operative specimens of the stomach, sigmoid colon, and rectum, demonstrating the visualization of the lymph nodes following clarification.

AGE AND METASTASES

The view that neoplasms tend to be more malignant in the younger age groups was substantiated by this study. In dividing the cases into two groups, those above and those below 50 years of age, the patients in the latter group had the higher incidence of metastases. Seventy-seven per cent of the gastric carcinomas in patients below 50 years of age had metastasized, in comparison to 75 per cent of those above; 75 per cent of the colonic cases in the younger age group had metastasized, in comparison to 55.8 per cent in the older age group, and 70 per cent of the rectal carcinomas in the first group had metastasized in comparison to 60.6 per cent in the second.

TABLE I

LOCATION	NUMBER OF CASES	AVERAGE NO. OF NODES PER SPECIMEN	AV. NO. NODES PER SPECIMEN IN GROUP WITH METASTASES	AV. NO. NODES PER SPECIMEN IN GROUP WITHOUT METASTASES	INCIDENCE OF REGIONAL LYMPH NODE METASTASES
Stomach	53	30.20	32.8	22.4	75.50
Colon	46	52.07	59.4	41.4	60.87
Rectum	53	67.00	66.2	67.5	64.20

DURATION OF SYMPTOMS

There was no relation between the duration of symptoms and the presence of lymph node metastases. It was noted that duration of symptoms diminished progressively from the stomach downward. The period between the onset of symptoms and the time of seeking medical

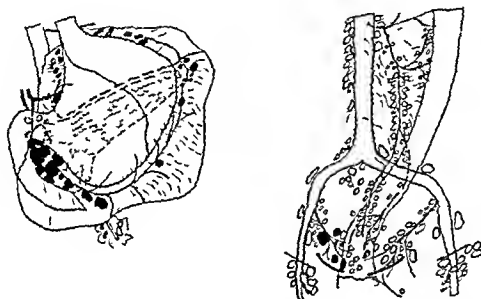


Fig. 2.—A, Line drawing demonstrating the zonal distribution of the lymphatic metastases in the necropsy specimen of a carcinoma of the stomach, B, line drawing of a necropsy specimen of a carcinoma of the anal canal, demonstrating the lateral zone of metastases

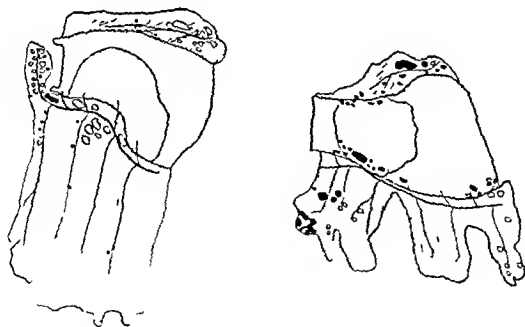


Fig. 3.—Line drawings of operative specimens of carcinoma of the stomach demonstrating variations in the incidence and zonal distribution of the lymphatic metastases

aid was longest in the stomach group. The average duration of symptoms was 13 months in the gastric group, 10 months for the colonic group, and 8 months for the rectal group. The patients with the shortest duration of symptoms do not always have the most favorable prognosis. Many of these carcinomas are fast growing and produce symp-

toms early. Many patients with symptoms present over a long period often have a more favorable prognosis. These are cases in which the neoplasm is slow-growing, is of a low degree of malignancy, and metastasizes late. Review of the histories of the 53 patients with carcinoma of the stomach revealed 5 with symptoms over a year's duration, who were free from lymphatic metastases. Several of these had had symptoms for two and three years, while 6 patients with symptoms ranging from one to three months had regional lymph node involvement. There was an incidence of lymphatic metastases in the colonic group of only 40 per cent (4 of 10 cases) in patients who had had symptoms for

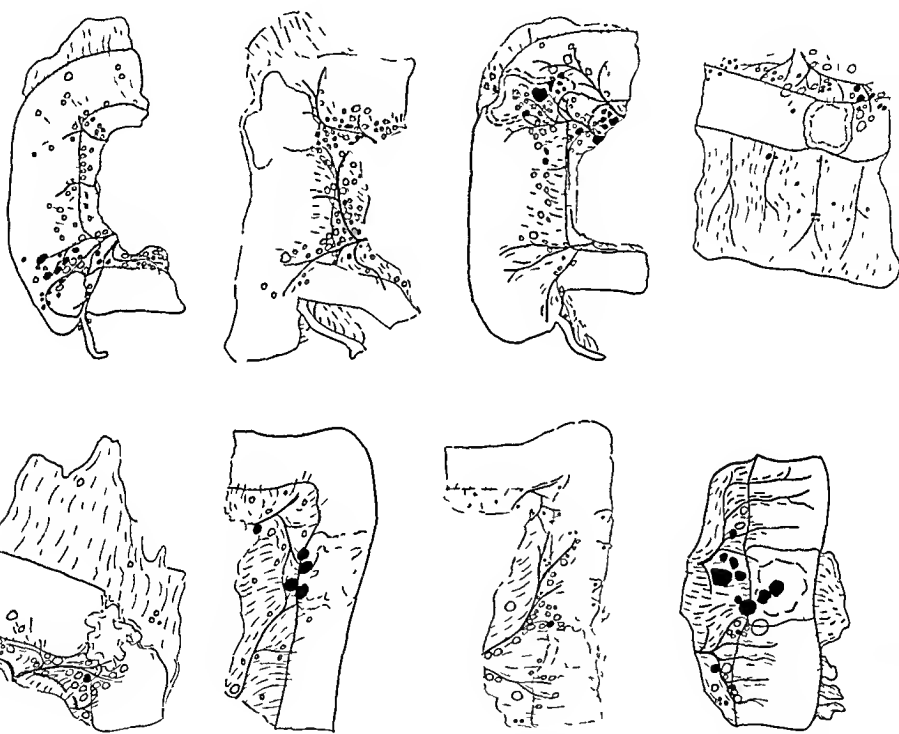


Fig. 4.—Line drawings of representative cases of operative specimens of carcinomas located in the various regions of the large intestine demonstrating the incidence and routes of their lymphatic metastases (Courtesy of *Annals of Surgery*.)

two years or more, in contrast to an incidence of 73 per cent metastases (8 of 11 cases) in patients with symptoms of three months or less. Similarly, in the rectal series there were 3 patients with symptoms of one month or less who had had lymph node metastases. There were several other patients without any symptoms who were found to have rectal carcinomas which were later discovered to have metastasized. There were 4 patients with symptoms of one year's duration, one of one and one-half year, and another of two years, all of whom were free

from lymph node metastases. One of these patients had been given up as hopeless one and one-half years prior to admission to this hospital. These observations show that operative procedures should not be minimized because of short duration of symptoms and that patients with symptoms over a long period of time should not be denied operation because of this fact alone.

GROSS TYPE AND METASTASES

Carcinomas of the gastrointestinal tract were classified according to their gross characteristics into three groups: (1) Neoplasms characterized primarily by the presence of ulceration; (2) the polypoid, fungating neoplasms which tend to grow intralumenly; and (3) the sessile, plaque-like neoplasms which are invasive in character. In the stomach series, there were 6 neoplasms of the ulcer type, of which 2 were found microscopically to have arisen upon peptic ulcers, and a third

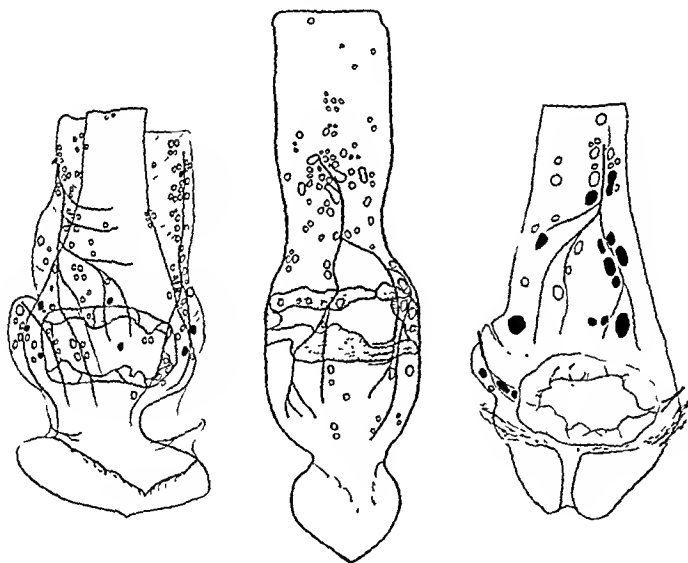


Fig. 5.—Line drawings of representative cases of operative specimens of carcinomas of the rectum demonstrating several of the variations noted in their lymphatic metastases.

in association with two nearby peptic ulcers. There were no cases in the colonie series within this group, and only three rectal neoplasms of the ulcer type. These were all large excavating ulcers. The polypoid neoplasms formed the largest group. There were 25 polypoid neoplasms of the stomach, 40 of the colon, and 28 of the rectum. The sessile neoplasms formed the intermediate group in regard to incidence. There were 22 sessile neoplasms of the stomach, 6 of the colon, and 21 of the rectum.

The 9 ulcer cases form too small a group from which to draw conclusions, but it is of interest to know that 66.6 per cent of the ulcer type in the stomach, and 33.3 per cent of those in the rectum had regional lymph node metastases.

In the polypoid group there was an incidence of metastases of 60 per cent in the stomach, 57.5 per cent in the colon, and 53.5 per cent in the rectum, while in the sessile group there was an incidence of metastases of 95.4 per cent in the stomach, 83.3 per cent in the colon, and 80.9 per cent in the rectum. It is of further interest to note that the incidence of sessile neoplasms in the gastric group (Table II) is much higher than it is in the other two groups, and that the incidence of polypoid neoplasms in the colonic group is the highest. As might be expected, the incidence of metastases is greatest in the gastric group and least in the colonic. Because of the above facts, it is mandatory that operative resections include all of the regional gland-bearing areas in cases of sessile neoplasms. Even though the incidence of metastases is less with the polypoid neoplasms, there is no method of determining which have or have not metastasized, consequently, they too must be observed with suspicion.

TABLE II
INCIDENCE OF METASTASES

	STOMACH	COLON	RECTUM
Ulcer	6 (66.6 per cent)	0 (0.0 per cent)	3 (33.3 per cent)
Polypoid	25 (60.0 per cent)	40 (57.5 per cent)	28 (53.5 per cent)
Sessile	22 (95.4 per cent)	6 (83.3 per cent)	21 (80.9 per cent)

SIZE AND METASTASES

There was no relation between the size of the neoplasm and the presence of metastases. It is of interest to note that the small neoplasms were just as likely to metastasize as the larger ones. In order to arrive at a more accurate figure concerning their relative sizes, their areas were computed rather than using references to any one diameter. The carcinomas of the cecum were the largest neoplasms of the entire gastrointestinal tract, averaging 46.56 sq. cm. The next largest were found in the stomach, which averaged 42.45 sq. cm. The neoplasms of the right colon were larger than those of the left. The average size of neoplasms with metastases in the right colon was 32.75 sq. cm. in comparison to 39.5 sq. cm. in those without, while the average of the neoplasms of the left colon with metastases was 22.11 sq. cm. compared to 31.73 sq. cm. in those without. This demonstrates that the incidence of metastases may be just as great, or greater, in the small neoplasm as in the large. The comparison, of course, eliminates automatically the large inoperable carcinomas. The smallest carcinomas were those in the rectum, which averaged 26.2 sq. cm. Differences in the size of the neoplasms above are not

the result of any inherent factor within the neoplasm, but rather the result of the location in which the neoplasm is found. The neoplasms of the cecum were the largest, because the caliber of the cecum is the largest, and neoplasms may exist there a long time before producing symptoms.

Analysis of the sizes of individual neoplasms shows those occurring in the fundus of the stomach to be considerably larger than any of the others, but when the areas of these were averaged with the smaller neoplasms occurring at the pylorus, the average for the entire gastric group was then second in size to those of the cecum. It is to be expected that neoplasms of the rectum are the smallest because of their clinical behavior and their accessibility to medical examination.

Further analysis of the data further revealed that in the gastric group 84.7 per cent of the neoplasms larger than average size had metastasized, compared to 66.6 per cent of those smaller than average size. Furthermore, 5 of the 6 largest neoplasms, and 4 of the 6 smallest neoplasms were found to have metastasized. In the rectal group, the 10 smallest and the 10 largest carcinomas were compared, and in each group there were 6 cases with and 4 cases without metastases. Thus, the size of the neoplasm is no indication of metastases.

CIRCUMFERENCE INVOLVED AND METASTASES

It is of interest to note the comparison in the amount of circumferential spread of the neoplasm in the rectum and the colon. Since the lymph channels follow the course of the intramural radial blood vessels around the circumference of the bowel, carcinomas of the rectum and colon tend to be annular. The carcinomas of the rectum were divided into four groups, depending upon the percentage of bowel circumference infiltrated. As will be seen from Table III, there was an increasing tendency to metastasize as more bowel circumference was involved.

TABLE III

PERCENTAGE OF CIRCUMFERENCE INVOLVED	NUMBER OF CASES	WITH METASTASES	PERCENTAGE METASTASES
0- 25 per cent	4	2	50.0
25- 30 per cent	10	6	60.0
50- 75 per cent	22	14	63.6
75-100 per cent	17	12	70.6

Many of the rectal neoplasms had only infiltrated from one-fourth to one-half of the bowel circumference, and 4 of them had involved less than one-fourth of the circumference.

In contrast, there were none of the colonic group with less than 25 per cent of the circumference involved and the majority of the neoplasms (37 out of 46) were completely annular. In only 3 instances was less than 50 per cent of the lumen involved, and 3 were included in the group

The 9 ulcer cases form too small a group from which to draw conclusions, but it is of interest to know that 66.6 per cent of the ulcer type in the stomach, and 33.3 per cent of those in the rectum had regional lymph node metastases.

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TABLE V

LOCATION	INCIDENCE OF GRADE I CARCINOMAS	INCIDENCE OF GRADE II CARCINOMAS	INCIDENCE OF GRADE III CARCINOMAS	INCIDENCE OF GRADE IV CARCINOMAS	INCIDENCE OF OF METASTASES
Colon	0	78.2	19.5	2.1	60.87
Rectum	0	62.2	33.9	1.8	64.2
Stomach	1.8	20.7	58.5	18.8	75.5

colon, rectum, and stomach (Table V). The majority of colonic neoplasms were grade II, or 78.2 per cent, compared to 19.5 per cent grade III carcinomas. The incidence of lymphatic metastases in the colon was 60.87 per cent. In the rectal series the incidence of grade II carcinomas had decreased to 62.2 per cent and grade III carcinomas had increased to 33.9 per cent. The incidence of metastases had also increased to 64.2 per cent. The carcinomas were even more undifferentiated in the gastric group, the majority being grade III. The incidence of grade II carcinomas had decreased to 20.7 per cent, the grade III carcinomas had increased to an incidence of 58.5 per cent, and for the first time there was an appreciable number of grade IV carcinomas, an incidence of 18.8 per cent. The incidence of metastases in the gastric group had also increased to 75.5 per cent.

MICROSCOPIC TYPE AND METASTASES

The majority of the neoplasms were proved histologically to be simple adenocarcinomas. This type composed 16 of the 53 gastric cases, 29 of the 46 colonic cases, and 31 of the 53 rectal cases. The medullary adenocarcinomas had the highest incidence of metastases, 100 per cent in the gastric group and 80 per cent in the colonic group. There were no medullary adenocarcinomas in this particular series of rectal neoplasms. In the gastric group, the scirrhous adenocarcinomas also had an incidence of metastases of 100 per cent. The carcinomas diagnosed adenocarcinoma mucosum also had a high incidence of metastases, 85.7 per cent in the gastric series, 100 per cent in the rectal series, and 75 per cent in the colonic series. The two groups having the lowest incidence of metastases were the adenocarcinomas (simplex) and the papilliferous adenocarcinomas. The adenocarcinomas (simplex) had an incidence of metastases of 56.25 per cent in the gastric group, 62.07 per cent in the colonic group, and 61.2 per cent in the rectal group, while the papilliferous adenocarcinomas had an incidence of metastases of 42.85 per cent in the gastric series, 37.5 per cent in the colonic, and 61.5 per cent in the rectal series.

SUMMARY

An analysis is presented of the incidence of lymphatic spread of 152 carcinomas of the gastrointestinal tract obtained by the dissection of cleared specimens.

of 75 to 100 per cent circumferential involvement. Because of the large number of completely annular carcinomas in the colon, the relation between circumferential involvement and metastases is not striking. However, of the 3 cases with 25 to 50 per cent involvement of the circumference, only 1 had metastasized.

DEPTH OF INFILTRATION AND METASTASES

Gabriel, Dukes, and Bussey⁵ classified carcinomas of the rectum into Groups A, B, and C. Group A included carcinomas infiltrating well into the wall but not into the perirectal tissues; Group B, those extending into the perirectal tissue; and Group C, those having positive lymph node metastases. The patients in 91 per cent of Group A cases and 64 per cent of Group B cases were alive five years or more following operative removal, whereas only 18 per cent survived five years in Group C. There were 30 cases in our series in which the malignancy was confined to the rectal wall and of these, 13 (43.3 per cent) had metastasized to the regional lymph nodes; whereas, there were 22 cases with infiltration into the perirectal tissues, of which 20 (90.9 per cent) had metastasized.

The contrast between the malignant character of the carcinomas of the rectum and those in the colon and stomach is striking. It was shown above that neoplasms of the colon had involved the entire circumference of the bowel in the majority of cases, compared to partial circumferential infiltration in the rectal group. It is noted here that the majority of the rectal neoplasms (30 of 53 cases) had not infiltrated through the bowel wall, while 47 of the 53 gastric cases, and 43 of the 46 colonic cases had infiltrated completely through their respective walls and involved the serosa. This is an ever-present source of free peritoneal metastases and may well be responsible for the better prognosis in carcinoma of the rectum. In 2 of the 5 gastric neoplasms, and 2 of the 3 colonic neoplasms in which the carcinomatous infiltration was confined to the muscular layer only, metastases were also found.

DEGREE OF CELLULAR DIFFERENTIATION (GRADING) AND METASTASES

Our studies (Table IV) substantiated the dictum that the more anaplastic the neoplasm, the higher the incidence of lymphatic metastases.

TABLE IV

GRADE	NUMBER OF CASES	NUMBER OF CASES	PERCENTAGE
	1	0	0.0
1	70	47	67.1
2	58	43	74.1
3	12	11	91.8
4			

The increasing incidence of metastases proceeding from the colon and rectum to the stomach is shown in Table IV. There was also an increasing incidence of neoplasms of the higher grading in the same order of

A DOUBLE TUBE METHOD FOR DRAINAGE AND FEEDING FOLLOWING GASTRIC RESECTION OR GASTROENTEROSTOMY

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(From the Graduate School [Surgical Division], New York Medical College, Flower-Fifth Avenue Hospital; Metropolitan Hospital)

DURING recent years a number of tubes have been devised and advocated for use in the postoperative care of patients undergoing gastric resection or gastroenterostomy. The simplest of these methods is the introduction of a Levin tube into the stomach to which suction is applied usually by means of a Wangensteen suction-drainage system. The advantage of this method is its simplicity and the prevention of gastric distension. However, it will not prevent distension of the very important afferent intestinal loop, neither is it effective for decompression of efferent small intestine, unless it is passed through the anastomotic stoma. This system has the further disadvantage of not permitting early nutritious feeding by means of a jejunal tube.

To offset the disadvantages of this method Abbott and Rawson¹ introduced their double lumen tube, the distal 30 cm. of which is a single lumen tube. This tube is passed into the stomach prior to operation and on completion of the anastomosis the terminal 30 cm. is manipulated into the efferent small intestine (Fig. 1). This tube permits constant gastric suction and early jejunal feeding. Efferent intestinal drainage may be obtained through the lumen used for jejunal feeding. The disadvantage of this tube is that there is no provision for suction drainage from the afferent intestinal loop.

Wangensteen² advocates a single lumen tube with forked ends (Fig. 2). This tube permits simultaneous drainage of both afferent and efferent intestinal loops. It makes no provision for early feeding of the debilitated patient by jejunal tube. Fluids introduced through this tube would be equally distributed to afferent and efferent loops.

Based upon the Abbott-Rawson and Wangensteen tubes we have formulated a method at the Metropolitan Hospital, which we believe combines the advantages of each without possessing the disadvantages of either. Use is made of two simple Levin tubes, size 12 F (Fig. 3). These are securely fastened together by means of fine black silk at a point 45 cm. from the tip of tube A and 30 cm. from tip of tube B. At a second point 15 cm. proximal they are again whipped together with black silk. Additional perforations, usually about twelve in number, are added to tube B equally placed from the tip proximally for 45 cm.

An average of 30.2 nodes per specimen was isolated in the gastric, 52 in the colonic, and 67 in the rectal series. A considerably larger number of lymph nodes per specimen was obtained in this way than is possible by the usual method of manual dissection.

An incidence of lymphatic metastases of 75.5 per cent was found in the gastric group, 60 per cent for the colonic, and 64.2 for the rectal.

The view that neoplasms in the younger age groups tend to have a higher incidence of metastases was substantiated by this study.

There was no relation between the duration of symptoms and the presence of lymph node metastases. A comparison of the incidence of lymphatic metastases in carcinoma of the gastrointestinal tract classified according to their gross characteristics, showed that the sessile neoplasms had a much greater tendency to metastasize than the polypoid neoplasms. In the polypoid group there was an incidence of metastases of 60 per cent in the stomach, 57.5 per cent in the colon, and 80.9 per cent in the rectum, while in the sessile group, there was an incidence of metastases of 95.4 per cent in the stomach, 83.3 per cent in the colon, and 80.9 per cent in the rectum.

There was no relation between the size of the neoplasm and the presence of metastases; the smaller neoplasms had just as high an incidence of metastases as the larger ones.

Our studies substantiated the dictum that the more anaplastic the neoplasm, the higher the incidence of lymphatic metastases.

The medullary adenocarcinomas and the adenocarcinoma mucosum had the highest incidence of metastases, while the adenocarcinomas (simplex) and the papilliferous adenocarcinomas had the lowest incidence of metastases.

REFERENCES

1. Collier, F. A., Kay, E. B., and McIntyre, R. S.: Regional Lymphatic Metastases of Carcinoma of the Rectum, *SURGERY* 8: 294, 1940.
2. Collier, F. A., Kay, E. B., and McIntyre, R. S.: Regional Lymphatic Metastases of Carcinoma of the Colon, presented at the Meeting of the Southern Surgical Association, New Orleans, Dec. 12, 1940.
3. Collier, F. A., Kay, E. B., and McIntyre, R. S.: Regional Lymphatic Metastases of Carcinoma of the Stomach. (In press.)
4. Gilchrist, R. K., and David, V. C.: Lymphatic Spread of Carcinoma of the Rectum, *Ann. Surg.* 108: 621, 1938.
5. Gabriel, W. B., Dukes, C., and Bussey, H. J. R.: Lymphatic Spread in Cancer of the Rectum, *Brit. J. Surg.* 23: 395, 1935.

tinal loop, and tube B is passed 30 cm. into the afferent loop. No difficulty is encountered identifying the tubes because of the unequal length of their terminal tips. If aseptic anastomosis is to be performed a tube with a metal bucket may be substituted for tube A for identification.

On completion of the operation and return of the patient to his room, constant suction by means of a 3-bottle Wangensteen is applied to tube B for drainage of the afferent intestinal loop, and maintained for at least seventy-two hours. To insure patency of the tube and prevent occlusion of lumina, 10 c.c. of normal saline solution are instilled every hour. Suction drainage by this tube prevents distension of the afferent loop and guards against closed loop duodenal obstruction that Wangensteen has emphasized. By its added perforations it permits gastric drainage and prevents distension proximal to the anastomosis. Tube A is used for jejunal feeding or efferent loop drainage. Immediately upon return of the patient from the operating room jejunal feeding is begun in the form of a continuous drip regulated so that the patient will receive 1000 c.c. every eight hours. To this feeding may be added gastric and duodenal contents suctioned off by tube B. Jejunal feeding is continued for at least seventy-two hours and the patient is also permitted clear fluids by mouth as soon as desired. Additions are rapidly made and when the patient can take a well-balanced diet by the oral route, jejunal feeding is discontinued. Jejunal feeding may be interrupted and suction applied to this tube whenever it becomes necessary for intestinal decompression. Before the tube is removed it is clamped for a test period and if the patient's progress is satisfactory it is then withdrawn.

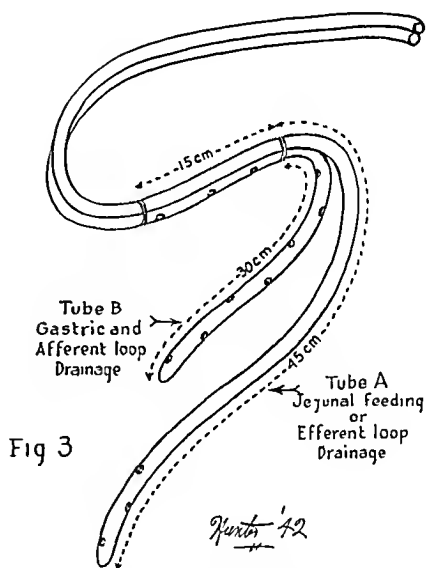
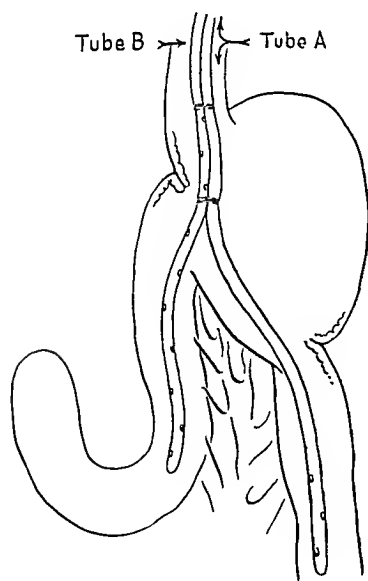
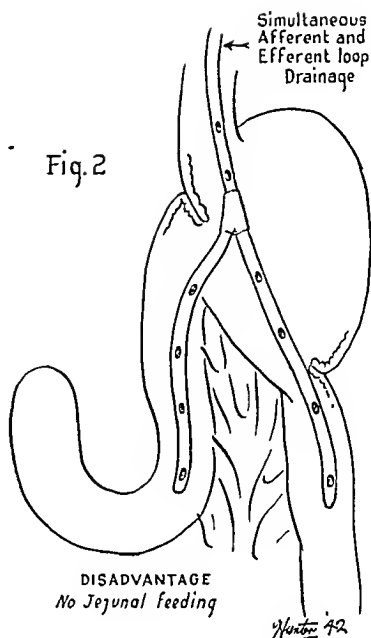
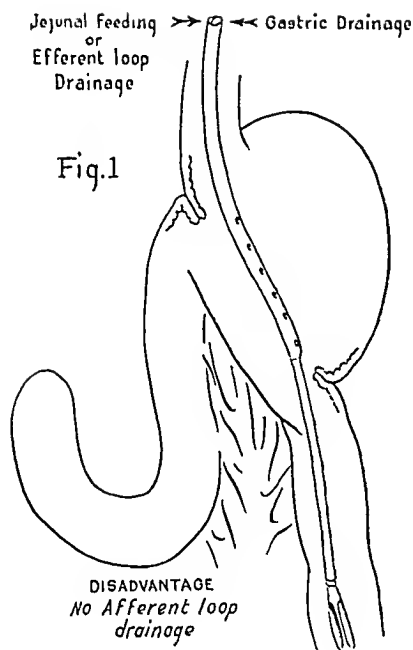
The advantages of early feeding to the debilitated patient are obvious. The patient receives nutrition with a carbohydrate, protein, and fat distribution that is impossible by the intravenous route; the danger of overloading the circulatory system is avoided, particularly in the old age group, which is often done when intravenous fluids are administered; additional medications may be introduced with facility through the jejunal tube.

SUMMARY

A simple double tube method for drainage and feeding following gastric resection or gastroenterostomy is presented. This method provides for constant and simultaneous gastric and afferent loop drainage. Early continuous jejunal feedings may be instituted. Discontinuing jejunal feedings provision is made for efferent loop decompression.

REFERENCES

1. Abbott, W. O., and Rawson, A. J.: Tube for Use in Postoperative Care of Gastroenterostomy Patients, *Correction*, J. A. M. A. 112: 2414, 1939.
2. Wangensteen, O. H.: Aseptic Resections in Gastrointestinal Tract With Special Reference to Resection of Stomach and Colon, *Surg., Gynec. & Obst.* 72: 257-281, 1941.



The proximal ends are clearly labeled Feeding, on tube A, and Drainage, on tube B. This double tube is passed through the nose into the stomach prior to operation in the usual manner. To facilitate its passage the tip of tube B may be moored to tube A with black silk. Before completing the anastomosis tube A is passed 45 cm. into the efferent intes-

tinal loop, and tube B is passed 30 cm. into the afferent loop. No difficulty is encountered identifying the tubes because of the unequal length of their terminal tips. If aseptic anastomosis is to be performed a tube with a metal bucket may be substituted for tube A for identification.

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THE POTENTIAL CLOSED DUODENAL LOOP IN GASTRIC RESECTION*

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THE occurrence of obstruction at the efferent outlet after gastrojejunal anastomoses is well known. Apart from a few reported instances of gangrene of the proximal afferent loop following gastrojejunal anastomoses, the occurrence of obstruction at the afferent inlet appears to have escaped the notice of surgeons as well as pathologists. In 1936, an instance of rotation of the proximal afferent jejunal loop with ensuing gangrene of the duodenojejunal loop, after an extensive resection for gastric carcinoma, was observed. The patient, Mr. C. B. (University Hospital No. 653763), died seventy-two hours after operation. The duodenum and afferent jejunal loop were distended and discolored. The serous surface of the bowel, in places, was torn. An ante-mortem blood culture as well as cultures taken from the peritoneal cavity and the bile in the gall bladder showed hemolytic streptococci.

In the intervening years, three additional patients have been seen, who came to autopsy presenting evidence of distention of the afferent duodenojejunal loop just proximal to the gastrojejunal anastomosis. In two of these, a gastric resection employing a retrocolic, Hofmeister plan of re-establishing gastrointestinal continuity had been done, in one instance for an obstructive duodenal ulcer, in the other, for gastric carcinoma. In the remaining patient, a posterior gastrojejunostomy had been made for a patient with a duodenal ulcer exhibiting high-grade pyloric obstruction. There was no suggestion of gangrene of the afferent duodenojejunal loop in any of these three patients, only distention of this loop without obvious cause. These three patients exhibited hyperthermia, tachycardia, and gradual decline of the blood pressure, followed by death within eighty hours after operation. The postoperative sequence of events was very much the same in each instance. The first two patients, in which this sequence of events obtained, were exceedingly poor risks and the finding of a patulous afferent inlet, despite the presence of a dilated proximal jejunal loop, persuaded the pathologists that this dilatation was without special significance. When, however, a third good-risk patient succumbed under similar circumstances, members of the surgical staff were convinced that such

*The researches presented here were supported by grants of the Graduate School of the University of Minnesota, the Citizens Aid Society, the Augustus L. Searle Fund for Experimental Surgical Research, and by a grant for technical assistance by the Work Projects Administration, Official Project No. 165-1-71-121, Subproject No. 399.

†Captain, on active duty with the Army of the United States.

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dilatation of the proximal duodenojejunal, afferent loop after gastric resection in the Billroth II type of operation was an item of real significance in the fatal issue.

The possibility of this occurrence has been mentioned previously, together with description of a technical maneuver to prevent its occurrence.^{4,7} It is the purpose of this paper to point out that: (1) Dilatation of the proximal duodenojejunal loop after gastric resection may be followed by hyperthermia, vascular collapse, and death without the occurrence of gangrene in the loop, (2) Experimental obstruction of the duodenojejunal loop in the dog is followed by the same sequence of events; and (3) This occurrence in man is probably infrequent but is a far more serious complication than obstruction at the efferent outlet. Placement of an indwelling duodenal tube within the afferent loop at the time of operation obviates this potential hazard.

CASE HISTORIES OF PATIENTS DYING OF HYPERTHERMIA AND VASCULAR COLLAPSE DUE TO DISTENTION OF THE PROXIMAL DUODENOJEJUNAL LOOP

Summary of Case Histories—Mr S J S (U H No. 695813), aged 59 years, in excellent physical condition, without obstruction, and with only slight weight loss, was operated upon for cancer of the stomach May 31, 1940. A Hofmeister retrocolic anastomosis with entero anastomosis was made after excision of 85 per cent of the stomach. The operation, done under intratracheal cyclopropane anesthesia, was accomplished without incident. The lines of resection were found to extend beyond the microscopic boundaries of spread of malignancy. The patient's condition on return to the ward was good, the pulse being 80 and the systolic pressure 140 mm. Hg, the rectal temperature rose gradually to 106° F. and the pulse to 144 per minute (Fig 1). The blood pressure declined and was difficult to sustain despite transfusion of adequate amounts of blood and plasma. Death occurred forty eight hours after operation.

During the first twenty four hour period following operation, the oral intake was 250 cc. During the same time 600 cc. of a deeply bile stained fluid were aspirated from the stomach. During the next twenty four hour period, 500 cc. of fluid were ingested and 1,250 cc. of a faintly bile stained fluid was aspirated from the indwelling gastric tube.

Permission for post mortem examination was denied but examination of the peritoneal cavity through the abdominal incision immediately after death was allowed. The proximal jejunal loop was distended but appeared to have good color. It seemed to have become sharply angulated at the site of the gastrojejunal anastomosis. Both gastrojejunal stomas, as well as the entero anastomosis, were patulous.

The other two patients, Mr. M. P. (U. H. No. 651411), aged 53 years, and Mrs. R. D. (U. H. No. 681265), aged 57 years, had been observed in this clinic at earlier dates. Both patients had been ill over many years with tuberculosis and duodenal ulcer. Both patients had been hospitalized in tuberculosis sanatoriums over long periods. One, Mr. M. P., had an active lesion at the time of hospitalization for duodenal ulcer. However, both patients were essentially afebrile prior to operation. Both patients, in addition, had high grade duodenal obstruction and alkalosis from persistent vomiting. In each instance, the obstruction remained refractory to treatment on the medical service and the patients were transferred to the surgical service for operation. Both patients were operated upon without meeting adequately,

preoperatively, the caloric and nitrogen requirements of debilitated patients. In the instance of one, Mr. M. P., a posterior gastrojejunostomy was done; in the other, a Finsterer exclusion type of gastric resection was done with a Hofmeister retrocolic anastomosis. Both operations were done without special incident and in each instance the immediate recovery period was quite ordinary. Both patients had indwelling gastric duodenal tubes to which suction was applied.

After thirty-six hours, Mr. M. P. exhibited quickening of the pulse and elevation of temperature to 106° F. There was also auricular fibrillation and a drop in the blood pressure to shock level. The patient was bronchoscoped, it being believed that atelectasis was responsible for the unusual reaction. Death occurred seventy-nine hours after operation. Autopsy disclosed dilatation of the proximal duodenojejunal loop but there was no evidence of loss of viability. The gastrojejunostomas were competent and patulous. There was no evidence of peritonitis. The lungs revealed an extensive active tuberculosis and also purulent bronchitis. The brain appeared normal, grossly; microscopic examination failed to disclose any significant finding. Apart from tuberculosis of the lungs, the only other important histologic finding was the observation of areas of liver necrosis. It was believed that the poor physical condition of the patient contributed largely to the fatal issue.

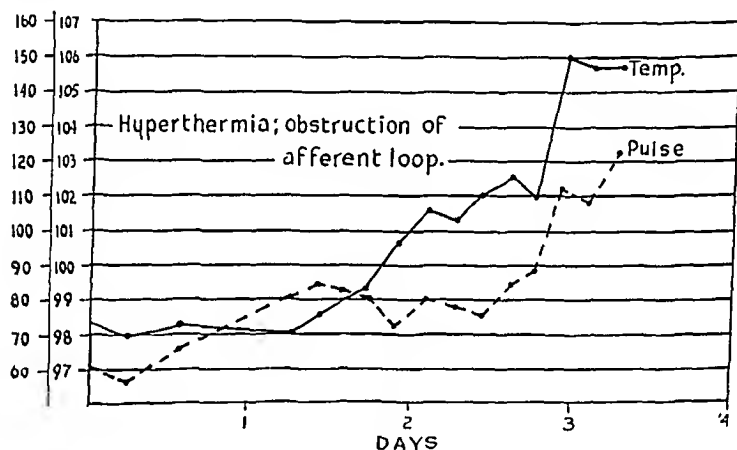


Fig. 1.—Hyperthermia attending obstruction of afferent gastrojejunal stoma in man.

The other patient, Mrs. R. D., exhibited a satisfactory convalescence for the first twenty-four hours, a pulse of 80 and a blood pressure of 130/80 having been sustained, with normal respiration. Following a chill, the temperature rose to 106° F. and the pulse accelerated to 120 beats per minute with a fall in blood pressure to 88/70. The patient remained in shock despite efforts to combat it. There were rales at the base of the right lung. Bronchoscopy was done without effect. Cyanosis deepened and tracheotomy was performed without improvement. The patient died thirty-nine hours after operation with hyperpyrexia, vascular collapse, and marked dyspnea. Autopsy disclosed extensive tuberculosis and bronchiectasis of the left lung. There was considerable edema of the right lung. There was an anomalous insertion of the bile duct into the duodenum. The liver was somewhat fatty. The proximal jejunal loop was distended, measuring 6 cm. in diameter. It contained a deeply bile-stained fluid. The loop appeared viable grossly. Microscopically the muscle was thin and somewhat fragmented. There were miliary abscesses in the portal spaces of the liver. Areas of the left lung exhibited fibrosis and the histologic findings of tuberculosis.

EXPERIMENTAL REPRODUCTION OF VASCULAR COLLAPSE AND HYPERTHERMIA
SYNDROME IN DOGS ATTENDING ESTABLISHMENT OF
A CLOSED DUODENAL LOOP

Method.—In thirteen dogs the following procedure was carried out. Under ether anesthesia and ordinary aseptic precautions, the duodenal loop was implanted subcutaneously in the manner of a Biebl skin-covered intestinal loop. Great care was observed not to injure the blood supply of the mobilized duodenal loop. Approximately ten days later, the duodenal loop was isolated by severing and inverting both ends. The experiment at this juncture being in the nature of an acute survival procedure, the continuity of the intestinal canal was not re-established.

The pressure in the loop was followed at intervals by introducing an 18 gauge needle through the skin directly into the subcutaneously implanted duodenal loop. The rectal temperature of the dog was recorded every four hours and he was allowed to wake up. In two animals, a No. 20 French urethral catheter was introduced into the distal end of the closed duodenal loop; in three dogs, a short closed duodenal loop, 10 to 15 cm. in length, was isolated, the bile and pancreatic ducts draining into the closed segment.

Results.—The results are summarized in Table I. It is to be noted that the survival time was considerably shorter than in the three patients noted above in whom only distention of the proximal duodenojejunal loop without obvious cause for the obstruction was noted. Fourteen of the animals showed an average maximum elevation of temperature of 105.2° F. In only one instance could the hyperthermia be explained on the basis of bronchopneumonia (Dog No. 17). In all instances save two (Dogs No. 9 and No. 17), the observed pressure in the closed duodenal loop exceeded that predicated by C. A. Dragstedt, Lang, and Millet (1929) to be necessary to arrest venous return from the duodenum. The average time intervening between observation of the critical duodenal intraluminal pressure noted by Dragstedt and his associates (see Fig. 3) and death of the animal was approximately fifteen hours.

The protein content of the peritoneal fluid was determined in a number of instances. It was invariably high. Values ranging from 4 to 6 Gm. per cent were usual, indicating that markedly increased capillary permeability was present. However, we were rather surprised to note that when a catheter was attached to a small fenestrated glass tube and placed in the peritoneal cavities in unobstructed dogs and cats, a peritoneal fluid with a high protein content was obtained, also. Usual values in these instances were concentrations of protein in the peritoneal fluid of 2.5 to 5 Gm. per cent.

DISCUSSION

That closed duodenal loops develop high intraluminal pressures is well known. Morton and Sullivan (1930) isolated closed intestinal

TABLE I
EFFECTS OF CLOSED DUODENAL LOOPS IN THE DOG

DOG NO.	LENGTH OF LOOP	MAXIMUM PRESSURE CM. H ₂ O	TIME OF MAXIMUM PRESSURE (HR.)	MAXIMUM TEMPERATURE	TIME OF MAXIMUM TEMPERATURE (HR.)	SURVIVAL (HR.)	CONDITION OF LOOP	MISCELLANEOUS
1	Entire duodenum	35 to 36.5	11	101°	12½	14	Loop intact, distended necrotic at antimesenteric border	Liver soft, friable, and congested
2	Entire duodenum	57 to 58	9	106°	11½	12½	As above	As above
3	Entire duodenum	27 to 40	5½	103°	7½	12	Intact, no distention, no gangrene	As above
4	Entire duodenum	33 to 78	12	104½	4½	52	Intact, distended, necrotic at antimesenteric border	As above
5	Entire duodenum	54 to 58	9½	103½	10½	18	Not intact, gangrene with perforation at distal end	Peritonitis
6	15 cm.	68.5	8	106½	22	24	Intact, distended, necrotic at antimesenteric border	Liver soft, friable and congested
7	15 cm.	65 to 68	35	106½	3½	46	As above	As above
8	Entire duodenum	17 to 54	8½	101½	7	10½	As above	As above
9	Entire duodenum	None	None	99	14	15	As above	Peritonitis
10	Entire duodenum	64 to 78	12	1047	6½	30½	As above	Liver soft, friable and congested
11	Entire duodenum	62	10	103½	29½	40	As above	As above
12	Entire duodenum	48	2	104	7	9	As above	As above
13	10 inches	42	2	101°	14½	22	Perforated at distal end at antimesenteric border	Peritonitis
14	Entire duodenum	41	18	107½	23	23	Necrotic at antimesenteric border; intact and distended	Liver soft, friable and congested
15	Entire duodenum	22	9	105½	16	16½	As above	As above
16	Entire duodenum	36 to 60	10½	101½	12½	12½	Open at distal end, no gangrene	Peritonitis
17	Entire duodenum	None	None	105½	24	24½	Intact, distended, necrotic at	Bronchopneumonia

loops 10 cm. in length in the ileum and duodenum, into which the biliary and pancreatic secretions did not drain. They noted that the intraluminal pressure and the amount of secretion in the closed duodenal loops far exceeded that of the closed ileal segments. That dogs with closed duodenal loops into which the biliary and pancreatic secretions drain, die with symptoms of vascular collapse and hyperthermia in just the same manner as may attend obstruction of the proximal afferent, duodenojejunal loop after the Billroth II type of operation in man, is significant. Inasmuch as the obstruction is complete in the dogs, it is understandable that the survival time is shorter than in the fatal instances observed after operation upon man. Harms (1927) observed, in cannulating the common bile duct and the main pancreatic duct in the dog, that secretion continued until pressures of 376 to 460 mm. of pancreatic juice and 309 mm. of bile were reached. Herring and Simpson (1906) observed secretory biliary pressures of 300 to 350 mm. of water. In short closed duodenal loops from which both biliary and pancreatic secretions were excluded, Morton and Sullivan observed secretory pressures of 300 to 370 mm. of water regularly. In one instance, the secretory pressure mounted to 520 mm. of water.

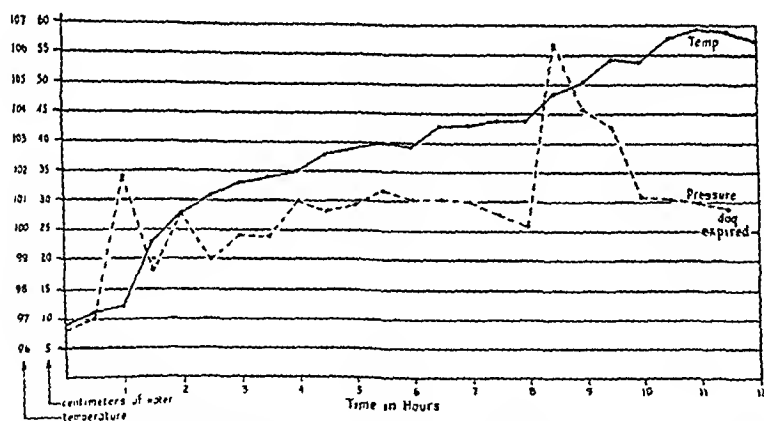


Fig. 2.—Hyperthermia attending closed duodenal loop obstruction in the dog (Table 1, Dog 2). The intraluminal pressure in the obstructed segment is indicated also.

Apart from the greater secretory pressures present in the duodenum, there is another item which makes this segment of the gut more susceptible to injury through the agency of increased intraluminal pressure than segments of ileum or colon. C. A. Dragstedt, Lang, and Millet (1929) have indicated that the manner of penetration of the circular muscle coat of the bowel by the mesenteric vessels differs considerably in various segments of the bowel. Ochsner and Storek (1937) have shown in a graphic manner, how a relatively small intraluminal pressure will obliterate the venous outflow from the duodenum, whereas far greater pressures are necessary to retard venous outflow from the colon (Fig. 3).

How obstruction of the afferent duodenojejunal loop comes about in man after gastric resection is not easy of appraisal. Elsewhere,^{8,9} it has been pointed out that obstruction at the efferent outlet in man after gastrojejunal anastomosis, comes about largely through the agency of overinversion of tissue by the surgeon. In the experience of this clinic, this is probably the sole cause of obstruction at the efferent outlet. It is very unlikely that such items as whether the proximal loop is iso- or antiperistaltic in direction with reference to its attachment to the stomach, whether it is short or long, what direction the incision in the gastric wall takes for the anastomosis—these factors are probably all

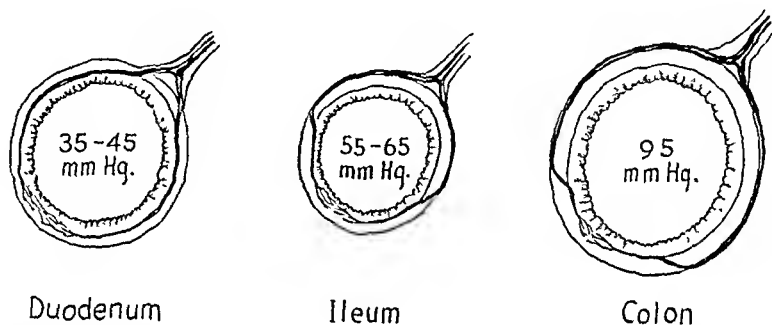


Fig. 3.—Venous obliteration at the afferent outlet. The pressure at various levels in the bowel. Owing to the immediate muscular coat by the vessels, at the mesenteric border (5 and 7 pressure will cause venous obliteration as contrasted with the colon, where the entry of the vessels is at 1 and 11 o'clock. In the ileum, the vessels enter at 3 and 9 o'clock. (Redrawn from Ochsner and Storck.)

inconsequential as far as the development of obstruction at the efferent outlet is concerned. The only thing that matters, apart from fixing the gastric stoma below the transverse mesocolon as Polya has emphasized in retrocolic anastomosis, is that the surgeon approximate a minimal amount of the adjacent walls of the stomach and jejunum in making the anastomosis. The experience of this clinic suggests that .5 to .75 cm. of the adjacent gastric and jejunal walls suffice to establish a satisfactory anastomosis (Fig. 4).

The most likely cause of obstruction, at the afferent outlet, on the contrary, is sharp angulation or kinking of the loop. And, unfortunately, as the recital of the cases mentioned in this report indicates, incomplete occlusion may bring about a fatal issue.

It is for this reason that we have come, in this clinic, to employ an indwelling duodenal tube extending into the proximal afferent inlet loop as a matter of routine in gastrojejunal anastomoses. In all probability, this complication of angulation at the afferent inlet does not occur often, yet, when it does occur, it is usually fatal. Maintaining the afferent channel widely patulous by the placement, at operation, of a fork of an indwelling duodenal tube into this limb of the gastrojejunal anastomosis assures continuity of this important channel.

Following observation of the instance of frank gangrene of the proximal duodenojejunal loop after gastric resection for carcinoma of the stomach in this clinic in 1936, it became routine practice for several years thereafter, to add an entero-anastomosis regularly in all resections for gastric malignancy. It is to be noted that, in the fatal issue reported

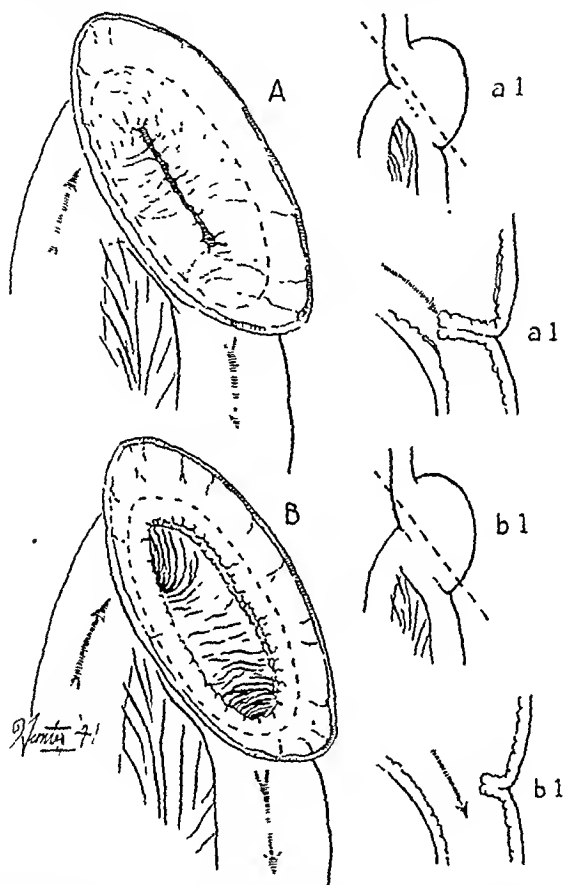


Fig 4—Mechanism of obstruction at the efferent outlet after gastrojejunal anastomoses. A, Inversion of too much tissue creates a flap, w/ outlet obstruction at the afferent inlet through such an stomal slit and obstructing flap. B, Inversion of too much tissue creates a flap, w/ outlet obstruction at the afferent inlet through such an stomal slit and obstructing flap. a1, Inversion of too much tissue creates a flap, w/ outlet obstruction at the afferent inlet through such an stomal slit and obstructing flap. b1, Inversion of too much tissue creates a flap, w/ outlet obstruction at the afferent inlet through such an stomal slit and obstructing flap. (Medico- Arnold Brunn, San Francisco, University of California Press, 1942)

here in the good-risk patient in which hyperthermia developed, an entero-anastomosis had been made and bile was obtained by suction from the inlying gastric tube, and yet distention of the proximal duodenojejunal loop occurred followed by death of the patient.

During recent years, all resections of the alimentary canal in this clinic, including gastric resections, have been made by the closed method. It is obviously a frank break in the aseptic technique to pull a straight

or forked catheter out from the residual gastric pouch through the gastrojejunal stoma in order to place the catheter or both limbs of a forked catheter into the afferent and efferent jejunal loops. Nevertheless, the experience of this clinic, with a large number of gastric resections for both ulcer and malignancy, suggests that this is an important expedient in obviating a potentially serious complication (Fig. 5).

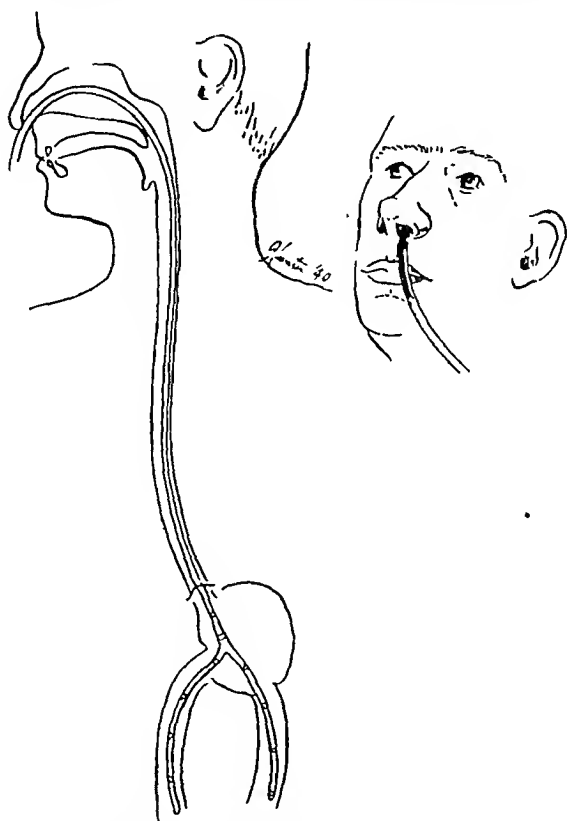


Fig. 5.—Forked catheter employed to prevent obstruction in the proximal jejunal loop after gastrojejunal anastomoses; one limb of the catheter is placed in the distal jejunal loop as well. Suction can be exerted simultaneously on the residual gastric pouch, the afferent and efferent limbs. A straight tube with multiple perforations inserted into the afferent loop meets the situation quite satisfactorily too. The tube is removed seventy-two hours after operation. (*Surg. Gynec. & Obst.* 72: 257, 1941.)

The safety of an operation depends upon leaving little to chance. Obstruction at the afferent inlet probably does not happen often and the causes which may provoke it are not entirely clear. On completion of the retrocolic antiperistaltic short-loop, Hofmeister gastrojejunal anastomosis, it is not uncommon to see the afferent loop assume a rather bizarre position, even with the transverse mesocolon anchored carefully to the stomach 1 cm. above the stoma. It affords the surgeon much comfort to know that a catheter in that loop will keep the duodeno-jejuno-gastric channel open during the early postoperative period.

SUMMARY

A syndrome of hyperthermia, vascular collapse, and death is described attending distention and partial obstruction without gangrene of the proximal duodenojejunal loop after gastric resection. Three cases are cited in which it is believed that distention of the proximal duodenojejunal loop was directly responsible for the fatal outcome.

When a complete closed loop obstruction is established in the duodenum of the dog, high secretory pressures ensue. Necrosis of the bowel is a regular accompaniment and perforation and gangrene are observed not uncommonly. The survival time is far shorter than that noted in man with distention occasioned by incomplete obstruction of the afferent duodenojejunal loop. Hyperthermia and vascular collapse attend, also, the closed loop duodenal obstruction of the dog. Death, in both man and dog, is owing, no doubt, to increased capillary permeability consequent upon a damaged bowel wall. Bacteria may migrate through the bowel wall to the peritoneal cavity or reach the liver via the duodenal veins.

The mechanism of obstruction at the afferent inlet after gastrojejunal anastomoses is not entirely clear. However, an effective means of preventing this unusual but serious potential postoperative complication is described.

REFERENCES

1. Dragstedt, C. A., Lang, V. F., and Millet, R. F.: The Relative Effects of Distension on Different Portions of the Intestine, *Arch. Surg.* 18: 2257, 1929.
2. Harms, E.: Über Druckmessungen im Gallen- und Pankreasgangsystem, *Arch. f. klin. Chir.* 147: 637, 1927.
3. Herring, P. T., and Simpson, Sutherland: On the Relation of the Liver Cells to the Blood-vessels and Lymphatics, *Proc. Roy. Soc., London, S. B.* 78: 455 1906.
4. Lynn, David H., Hay, Lyle J., and Wangensteen, O. H.: Hyperthermia and Death Caused by a Closed Duodeno-jejunal Loop After Gastric Resection: Prevention of the Complication; Experimental Reproduction of the Syndrome in the Dog, *Am. J. Path.* 17: 455, 1941 (Abstract).
5. Morton, J. J., and Sullivan, W. C.: Comparison Between Simultaneous Equalized Closed Obstructions of Duodenum and Ileum, *Arch. Surg.* 21: 531, 1930.
6. Ochsner, A., and Storek, A. H.: Mechanical Decompression of Small Intestine in Ileus; Clinical Observations With Report of Cases, *J. A. M. A.* 108: 260, 1937.
7. Wangensteen, O. H.: Aseptic Resections in the Gastrointestinal Tract: With Special Reference to Resection of the Stomach and Colon, *Surg. Gynec. & Obst.* 72: 237, 1911.
8. Wangensteen, O. H.: The Cause and Prevention of Stomal Obstruction in Gastrojejunal Anastomoses (Gastric Resection and Gastrojejunostomy), *Medico-Surgical Tributes to Harold Bruun*, San Francisco, 1942, University of California Press.
9. Wangensteen, O. H.: *Intestinal Obstructions*, Ed. 2, Springfield, Ill., 1942, Charles C Thomas.

THE TREATMENT OF ACUTE APPENDICITIS IN CHILDREN AS INFLUENCED BY CHEMOTHERAPY

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INTRODUCTION

SINCE the publication by Domagk,¹ 1935, dealing with the effects of prontosil on streptococcus infections in mice, treatment of such infections in man by chemotherapy or sulfonamide drugs has progressed rapidly. While in general a maximum therapeutic effect on some particular organism has been associated with a particular compound, evidence has accumulated to prove that the effective coverage of most of the compounds is wide enough to include a number of organisms. This is particularly true for those organisms associated with peritonitis secondary to appendicitis; namely, streptococcus, *Bacillus coli*, *B. welchii*, and certain other anaerobes. Infections in animals due to all these organisms have been shown to be influenced favorably by sulfanilamide, sulfapyridine, and sulfathiazole. These three drugs have been utilized as an aid to surgery in the treatment of appendicitis and its complications at the St. Louis Children's Hospital during the past four years. This paper is presented to show the results of such treatment. A comparison of the results in this period is made with those of a previous period of fifteen years' duration.

Others also, including Ravdin, Rhoads, and Loekwood,² 1940, Long and Dees,³ 1941, and Thompson, Brabson, and Walker,⁴ 1941, have reported improved results in the treatment of peritonitis associated with appendicitis through the use of the sulfonamide drugs.

GENERAL CONSIDERATIONS IN CHEMOTHERAPY

Most observers believe that the action of the sulfonamide compounds is one of growth inhibition or bacteriostasis. The newer drugs are capable of holding the invading organisms in check until antibodies are developed sufficiently to bring about bacteriolysis. A lag period of four to six hours has been shown to exist before the maximum effectiveness of the drugs becomes manifest.

It is our practice to administer the drugs prior to operation in all cases of appendicitis where peritonitis is diagnosed or even suspected. Experience has demonstrated that it is in the invasive stage, not in the chronic or entrenched stage, that chemotherapy is most effective. This is the basis for the belief that there is less danger in operating on patients with peritonitis than formerly, provided an effective drug is used

before, during, and for a limited period after the operation. There is no longer the great danger of a disastrous spread of the infection by operative procedures. It must be emphasized that chemotherapy in itself cannot be maximally effective where there is a continuing addition of infectious organisms or when pus is present in walled-off abscesses. Long-continued use of the drugs with delay in surgical drainage of abscesses is not only useless but actually may be harmful. In acute infections the drugs must be administered in sufficient amounts to bring quickly the concentration in the blood up to levels which have been found effective. The choice of drug dosage and administration intervals used by us is the result of extensive research by Hartmann and his associates,⁵ 1940, on chemotherapy.

DOSAGE

The blood levels found effective for sulfanilamide range from 8 to 14 mg. per cent, for sulfapyridine and sulfathiazole, 6 to 12 mg. per cent. To reach such levels quickly, 1.0 per cent sulfanilamide in normal saline solution, or a 5 per cent solution of the sodium salts of sulfapyridine or sulfathiazole, is given intravenously. Sulfanilamide, sulfapyridine, and sulfathiazole are administered on the basis of 0.2 Gm. per kilogram body weight in six divided doses. Sulfanilamide can be administered subcutaneously on the basis of 0.1 Gm. per kilogram body weight given twice a day in the form of an 0.8 per cent solution. When sodium sulfapyridine is given intravenously the dosage is 1 c.c. of the 5 per cent solution per kilogram body weight repeated every eight hours; for sodium sulfathiazole 2 c.c. of 5 per cent solution per kilogram body weight every six hours, as it is excreted much more rapidly. Occasionally 2 to 5 Gm. of sterilized powdered sulfanilamide have been placed locally in an abscess cavity or in the area from which an adherent gangrenous appendix has been removed, or in the muscle layer during closure in an infected or potentially infected appendix.

COMPLICATIONS

Complications from the use of the drugs in children are not severe or frequent. Nausea and vomiting develop in some patients. Usually during the period when the concentration of the drug must be maintained at a high level, gastric suction is also used, which tends to eliminate vomiting. In a few patients the dosage may have to be decreased to stop vomiting. In our series of cases no severe leucopenia or anemia has resulted. The presence of a leucopenia from a severe infection prior to treatment has not been a contraindication to the use of drugs. Renal bleeding occasionally is met with and usually is relieved by changing to another drug or lessening the amount of the drug being administered. In severely toxic patients, jaundice has followed the use of the drugs in a few cases. Cyanosis due to elevated methemoglobin concentration is often encountered. This can be counteracted by the intravenous ad-

ministration of methylene blue, using 1 to 2 mg. per kilogram body weight, or by the giving of 1 to 2 gr. every four hours as needed by oral route. It is deemed especially advisable to give methylene blue preoperatively at least one hour before an anesthetic. To help in the recognition of toxic effects of the drugs, daily blood studies, urinalysis, and methemoglobin determinations are done.

EFFECTS OF CHEMOTHERAPY

The beneficial effects attributable to chemotherapy in the treatment of the complications of appendicitis in children are: (1) a rapid lessening of the toxicity, (2) a rapid regression of the peritonitis, (3) a reduction in the number of cases requiring drainage, and (4) a shortening of the period of illness. The added effect has been practically to eliminate death as a sequel to peritonitis associated with appendicitis. Even though it is acknowledged that chemotherapy has improved greatly the prognosis in appendicitis, properly instituted surgery still plays the most essential role. The earliest possible removal of the source of continuing contamination of the peritoneal cavity is imperative. Chemotherapy alone cannot and should not be relied upon to cure infection of the peritoneal cavity from a gangrenous or ruptured appendix.

PREOPERATIVE CONSIDERATIONS

It is well recognized that before any operation is performed the fluid, electrolytic and nutritional deficiencies or derangements of the patient must be corrected. Protracted nausea and vomiting may be assumed to indicate a food and electrolytic deficiency. From blood studies, the hematocrit reading, blood chloride and plasma protein determinations, a more precise knowledge of these deficiencies can be procured.

The steps necessary to correct a loss of fluid and electrolytes are well known. In children the dosage of Ringer's solution is usually 50 to 60 c.c. per kilogram body weight, given subcutaneously; 20 to 30 c.c. of 10 per cent dextrose per kilogram body weight can be given intravenously to overcome food deficiency. It can be added to Ringer's solution when given intravenously or separately. Protein deficiency can be corrected by the administration of plasma, 30 c.c. per kilogram body weight. If plasma is not available casein digest in the form of a 5 per cent amino acid mixture with 10 per cent dextrose may be substituted (Elman,⁶ 1940). A child requires 2.5 Gm. of protein per kilogram body weight per day, the mixture given intravenously.

Usually two to six hours are required to prepare the patient for operation and if the case is severely toxic eight to twenty-four hours may be necessary.

OPERATION

During the operation, especially in toxic cases, the anesthetic must be administered carefully. Drop ether is employed. The patient is kept

as light as possible and cyanosis is avoided. In severely toxic cases an attempt is often made to open the abdomen under local anesthesia. Ether then is administered to permit adequate exposure to complete the operation quickly. *The appendix should always be removed.* Drainage is used only if abscess formation has injured the peritoneum locally. It is not used if the peritoneum is involved to the same degree diffusely. Chemotherapy makes the use of drains less frequently necessary. This, in turn, results in fewer instances of postoperative obstruction due to adhesions.

The operation usually is done through a low right rectus incision with retraction of the muscle in clean cases or splitting of the muscle in contaminated cases. The McBurney incision seldom is used unless a definitely localized abscess is present.

POSTOPERATIVE CARE

Postoperative chemotherapy is continued at a high level until the temperature subsides. This happens much sooner under such treatment than in those cases not treated with chemotherapy. Intravenous fluids, electrolytes, and nutritive substances are favored immediately after operation rather than the early administration of food by mouth. After the temperature subsides the drug is continued at one-half the previous dosage for three to five days. In all other respects the practices followed are those in general use.

ILLUSTRATIVE CASES

CASE 1.—An acutely ill boy, $4\frac{1}{2}$ years old, was admitted to the St. Louis Children's Hospital, Aug. 13, 1940. There was a history of abdominal pain, nausea, and vomiting of two days' duration. An enema had been given but no cathartic. Temperature at the time of admission was 38.1° rectally; respirations, 28; and pulse, 160. The skin was hot and dry, nasopharynx and chest findings were negative. Abdominal examination showed the child's legs drawn up as if in pain, with marked rigidity and localized tenderness below and to the right of the umbilicus. Definite rebound tenderness was present. Rectal examination was negative; urine, negative; W.B.C., 25,000.

A diagnosis of acute appendicitis with probable peritonitis was made. The patient was given 30 c.c. of 5 per cent sodium sulfathiazole intravenously (1.5 Gm.), as well as 200 c.c. of 10 per cent glucose intravenously, and 200 c.c. Ringer's solution subcutaneously. Four hours later the child was operated upon under drop ether anesthesia. The appendix was gangrenous in its distal third. Within the abdominal cavity a creamy exudate was encountered, which on culture revealed *B. coli*. The appendix was removed and the abdomen closed without drainage. Postoperatively, sulfathiazole and fluids were continued. On the third postoperative day the temperature was normal and the patient was on a soft diet. The wound healed by primary intention and the patient was discharged on the ninth postoperative day.

CASE 2.—A four-year-old colored girl was admitted April 20, 1940. There was a history of pain in the abdomen, nausea, and vomiting of four days' duration. The child had been given castor oil. Prior to entry the pain and vomiting became worse, the child became distended and drowsy. Temperature on admission, 38°

C.; respirations, 32; pulse, 126. Examination revealed a markedly toxic patient with a dry skin. The pharynx and chest findings were negative. The abdomen was distended markedly, dullness was present in the flanks, no sounds could be heard on auscultation, and some generalized tenderness was present. The white blood cell count was 5,200; urine, negative.

A diagnosis of acute appendicitis with peritonitis was made. Wangeensteen suction was instituted; intravenous and subcutaneous fluids were given. One gram of 1 per cent sulfanilamide in Ringer's solution was administered subcutaneously every four hours, or .4 Gm. per kilogram body weight per twenty-four hours. Twenty-four hours later operation was performed under drop ether anesthesia. When the peritoneum was opened there was a gush of foul-smelling pus and loops of ileum were found covered with a thick fibrinous purulent exudate. The appendix was lying free and had amputated itself at the base. The appendiceal stump was open. This stump was closed, drains were placed, and the abdomen was closed.

Nasal suction was instituted postoperatively. The child was given intravenous fluids, glucose, methylene blue, blood transfusions, vitamins and 1 per cent sulfanilamide subcutaneously. The sulfanilamide concentration the day following the operation was 24.6 mg. per cent. At this time the child was more alert and the temperature curve was starting downward. The nasal tube was removed on the third postoperative day, and the patient began taking broth and tea. On the sixth postoperative day the child was on a soft diet and was discharged as well, May 16, 1940.

CASE 3.—A white girl, 8 years old, was admitted Dec. 4, 1940, with a history of cramping abdominal pains, fever, chilly sensation, watery diarrhea and persistent vomiting of four days' duration. On entry to the hospital the child was restless and lethargic. She was markedly dehydrated and toxic. Temperature on admission, 38.8° C.; respirations, 42; pulse, 120. The color of the patient was dusky. The pharynx and lungs were clear. The right abdomen was diffusely tender and rigid; W.B.C., 22,000; urine, negative; and vaginal smear showed no pneumococci. Blood culture showed no growth.

The child was given fluids intravenously. Five per cent sodium sulfapyridine was administered intravenously every eight hours. After sixteen hours of observation and therapy the condition did not improve, even though the blood sulfapyridine determination was 11.3 mg. per cent.

A clinical diagnosis of peritonitis, the type undetermined, was made. Since the source might be a perforated appendix, an exploratory laparotomy was advised. This was done under local anesthesia, the child being very toxic and difficult to arouse. When the abdomen was opened, considerable congestion and edema of the appendix and intestines were found. Much fibrin and thick pus were present. A smear made immediately showed diplococci. These were identified subsequently as type one pneumococci. No Meckel's diverticulum was found. The appendix was removed and the abdomen closed without drainage.

Postoperatively, the patient was continued on sodium sulfapyridine. She was placed in an oxygen tent. Fluids and glucose were given intravenously; multiple transfusions were administered. On the fifth postoperative day she was taken out of the oxygen tent and was given fluids and medication by mouth. On the sixth postoperative day she developed a right lobar pneumonia followed by an empyema which later required drainage. She was discharged as well on Jan. 21, 1941.

This case while not one of appendicitis is presented because idiopathic peritonitis is differentiated, often with difficulty, from peritonitis secondary to appendicitis. The course followed in this case is the one recommended by us in all cases of peritonitis of doubtful origin. Exploratory

operation through a small incision is recommended rather than needling, because by the latter method fluid is not always obtained, and if fluid containing streptococci is obtained, the appendix still may be the primary cause of the disease. If the exploration reveals appendicitis the wound is enlarged to permit appendectomy, if not, the appendix usually is not removed.

STATISTICAL DATA

During the past four years, 1938-1942, at the St. Louis Children's Hospital there have been 223 appendectomies, or operations for appendicitis, with five deaths, a mortality of 2.2 per cent.

It is to be noted that no deaths occurred following operations for acute unruptured appendicitis, recurrent unruptured appendicitis, or acute

TABLE I
MORTALITY FOR DIFFERENT TYPES OF APPENDICITIS
(JANUARY, 1938, TO JANUARY, 1942)

TYPE	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
Acute, unruptured	102	0	0
Recurrent, unruptured	75	0	0
Acute, local peritonitis	14	0	0
Acute, diffuse peritonitis	32	5	15.6
Total	223	5	2.2

TABLE II
MORTALITY RATE ACCORDING TO CLASSES (1915-1932)

CLASS	TOTAL CASES	DEATHS	MORTALITY (PER CENT)
1	21	0	0
2	31	0	0
3	65	1	1.56
4	99	2	2.02
5	122	11(a)	9.02
6	42	16(b)	38.10
Total	380	30(c)	7.89

Apd acute Let respic asses (1) chronic, (2) recurrent, (3) subacute, (4) with abscess, (6) ruptured with peritonitis denote the inclusion of one, two, and three patients, operation

TABLE III
AGE INCIDENCE IN RELATION TO MORTALITY
(JANUARY, 1938-JANUARY, 1942)

AGE (Yr.)	SIMPLE APPENDICITIS (NUMBER OF CASES)	MORTALITY (PER CENT)	APPENDICITIS COMPLICATED (NUMBER OF CASES)	DEATH	MORTALITY (PER CENT)
1 to 3	5	0	5	2	40
3 to 6	14	0	9	2	22
6 to 9	31	0	8	1	12
9 to 12	69	0	11	0	0
12 to 15	58	0	10	0	0
Total	177	0	46	5	10

TABLE IV
ANALYSIS OF FATAL CASES

ADMISSION DATE	AGE (YR.)	DURATION OF ILLNESS (IN DAYS) BEFORE TREATMENT	PREOPERATIVE CHEMOTHERAPY	OPERATION	POSTOPERATIVE CHEMOTHERAPY	DATE OF DEATH	CAUSE OF DEATH
3/16/38	7	2	Adequate	Exploratory laparotomy; appendix not removed	Adequate	3/28/38	Peritonitis
7/25/38	2	8	None	Appendectomy	Very inadequate	7/26/38	Peritonitis
1/ 6/39	3½	8	Adequate	Exploratory laparotomy; appendix not removed	Adequate	1/15/39	Peritonitis
5/17/39	2	5	Adequate	Appendectomy with drainage	Adequate	7/16/39	Intestinal obstruction
7/25/39	3	2	None	Appendectomy	None	7/25/39	Death during operation. Anesthesia (?), peritonitis

appendicitis with local peritonitis. The five deaths which occurred resulted from appendicitis associated with diffuse peritonitis. There were thirty-two cases of diffuse peritonitis, making the mortality rate 15.6 per cent. During 1940 and 1941 there were no deaths at the St. Louis Children's Hospital from appendicitis or its complications. It was during this period that the principles governing the treatment of appendicitis, as outlined above, first were employed unfailingly.

In Table II are shown the results in cases of appendicitis during a previous period, 1915-1932, at the Children's Hospital as summarized by E. L. Keyes,⁷ 1934. Note a total mortality of 7.89 per cent instead of the present 2.2 per cent and a mortality of 38 per cent as compared to the present 15.6 per cent for cases with ruptured appendicitis with diffuse peritonitis.

In Table III the age incidence in relation to mortality is shown.

In Table IV an analysis of the five fatal cases during the 1938-1942 period is presented. The analysis indicates that peritonitis is the usual cause of death following appendicitis. It is felt definitely that the involved appendix should be removed. Inadequate exposure is often the only factor which prevents this.

SUMMARY

During the past four years at St. Louis Children's Hospital the mortality from acute appendicitis and its complications has been reduced from a previous average of 7.89 per cent to 2.2 per cent.

The improved results are ascribed essentially to the early removal of the appendix, to intensive and well-directed pre- and postoperative care, and to the adequate use of the sulfonamide drugs before and after operation.

During 1940 and 1941 there were no deaths from appendicitis.

The methods of administration of the sulfonamide drugs and the surgical principles governing the care of patients before and after operation are described.

The authors wish to express their appreciation to Dr. A. F. Hartmann and his associates for the cooperation of the medical service in this problem of appendicitis.

REFERENCES

1. Domagk, G.: Ein Beitrag zur Chemotherapie der bakteriellen Infektionen, *Deutsche med. Wchnschr.* 61: 250, 1935.
2. Ravdin, Isidor S., Rhoads, Jonathan E., and Lockwood, John S.: The Use of Sulfanilamide in the Treatment of Peritonitis Associated with Appendicitis, *Ann. Surg.* 111: 53, 1940.
3. Long, Lawrence W., and Dees, J. Gordon: The Local Use of Sulfanilamide, *Surgey* 9: 878, 1941.
4. Thompson, James L., Brabson, John A., and Walker, John M.: The Intra-Abdominal Application of Sulfanilamide in Acute Appendicitis, *Surg., Gynec. & Obst.* 72: 722, 1941.
5. Hartmann, A. F., Burnett, H. L., Perley, A. M., and Ruhoff, M. B.: Present Status of Therapy with Sulfanilamide and Sulfapyridine, *J. Missouri M. A.* 37: 41, 1940.
6. Elman, Robert: Parenteral Replacement of Protein With the Amino-Acids of Hydrolyzed Casein, *Ann. Surg.* 112: 594, 1940.
7. Keyes, E. Lawrence: Death From Appendicitis, *Ann. Surg.* 99: 17, 1934.

REPORT OF A CASE OF UNUSUAL ANOMALY OF THE BILE DUCTS IN AN ADULT WITH OBSTRUCTIVE JAUNDICE

O. W. NIEMMEIER, M.B., F.R.C.S., HAMILTON, ONT.

THIS case is of interest chiefly because of the unusual anomaly of the bile ducts found at operation and the technical difficulties and dangers incidental to this anomalous arrangement. The case also presents certain points of diagnostic interest.

The patient is a female, aged 51 years, who was admitted to the Hamilton General Hospital on April 7, 1940.

Past History.—She has had flatulent dyspepsia for twenty years. Nine months before admission she had an attack of indigestion which was followed by jaundice lasting two to three weeks. Another similar attack occurred three months before admission and again three weeks before admission.

The jaundice following the last attack persisted and increased until her entry into the hospital. She states that she had some epigastric discomfort in these attacks but no pain. She had lost twenty pounds in weight during the nine months previous to entering the hospital.

Complaints.—On admission, Mrs. M. complained of weakness, loss of weight, and jaundice.

Physical Findings.—Jaundice was very marked and was of the orange type. Stools were clay colored and the urine was dark. The liver was palpable one and one half inch below the costal margin and was smooth. The gall bladder could not be palpated and tenderness was absent. The spleen was not palpably enlarged.

Laboratory Findings.—Urine showed ++ bile, stools also showed traces of bile at times. Van den Bergh's test was direct +, indirect +++, icterus index was 99 on April 10, and gradually fell to 54 on April 25. Fragility test was normal and galactose tolerance test showed an excretion of 2 Gm.

X-ray Examination.—Flat plate and gastrointestinal series were negative. Because of the jaundice, iodikon was not used.

Discussion of Diagnosis.—Parenchymatous disease was ruled out by the galactose tolerance test and the absence of an enlarged spleen. Hemolytic jaundice was excluded by the normal fragility test.

Carcinoma of the head of the pancreas was excluded by the absence of an enlarged gall bladder, the fact that the jaundice was not extreme, was not complete, and was diminished rather than increased.

Stone in the common duct was suspected because of the long history of flatulent indigestion in spite of the absence of definite pain preceding the onset and laparotomy was advised.

Preoperative Preparation.—Vitamin K and bile salts were given until the prothrombin time was normal and fluids and glucose were administered freely.

Operation.—The gall bladder lay in its normal position attached to the under surface of the liver. It was distended and shaped somewhat like a dumbbell, consisting of two globular distended portions connected by a narrow waist. The lower pouch of the gall bladder contained a hard mass and was entirely covered by the peritoneal fold of the hepatoduodenal ligament (Fig. 1).

This overlying peritoneal fold was divided and reflected and dissection was carried out to expose the cystic hepatic and common bile ducts. A large duct was found entering the distended lower pouch of the gall bladder. This duct was three-eighths of an inch in diameter and as it passed down behind the duodenum was obviously the common duct (Fig. 2). No evidence of a cystic duct could be found. The fundus of the gall bladder was separated from the liver above and dissection was carried downward. The cystic vessels were encountered and ligated and another duct coming from above was found entering the distended lower pouch of the gall bladder on its upper aspect. This duct was about five-eighths of an inch in diameter (Fig. 3). The gall bladder was then opened to make sure we were not dealing with a densely adherent common duct (Fig. 5). A mass of small gall stones cemented together with puttylike material was removed from the distended

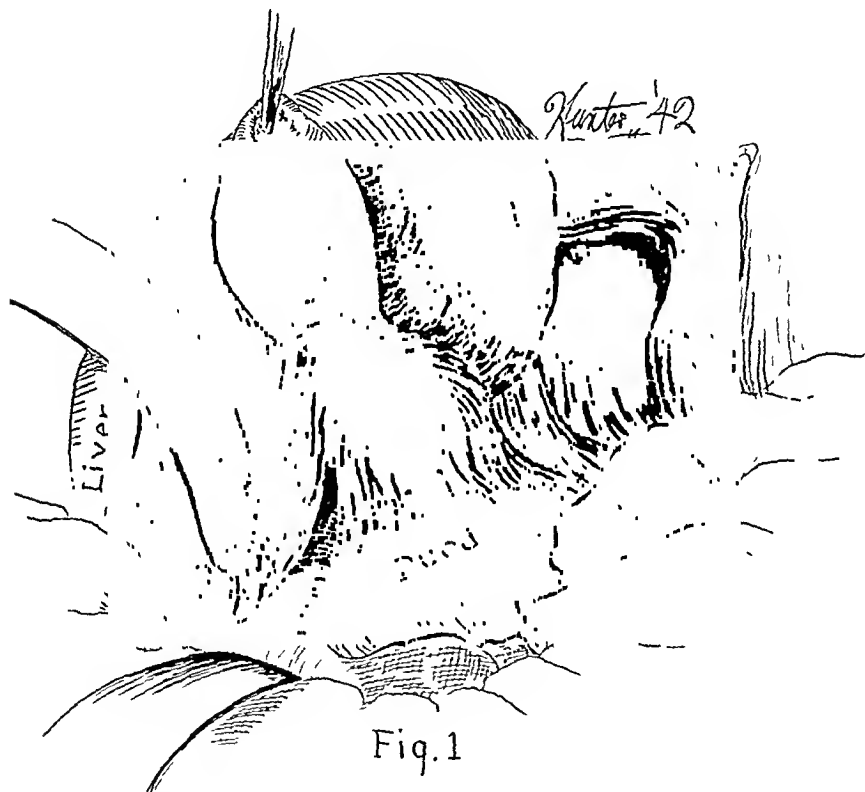


Fig. 1—Condition seen on exposing the gall bladder, note the distended lower pouch enveloped by the gastrohepatic ligament.

lower segment. The orifices of both ducts displayed by dissection could be seen from within the gall bladder and a probe was passed into these ducts. No other orifice could be found. The gall bladder formed the only connection between the common hepatic duct and the common bile duct, the cystic duct being absent (Fig. 6). We then had the following three alternatives: (1) Cholecystostomy; (2) partial resection, leaving the lower segment of the gall bladder; (3) complete cholecystectomy with subsequent anastomosis of the ducts (Fig. 7).

We chose the latter procedure, that is, uniting the ducts over a T tube. The tube was left in situ for several months and the patient has had no trouble since.

Specimen.—The specimen is a thick-walled gall bladder with two orifices at its lower end where the ducts were divided (Fig. 8). The ducts were divided as near the gall bladder as possible, leaving no stumps on the latter in order to preserve as much duct as possible for approximation. There was no segment of duct attached to the gall bladder, thus ruling out the dreaded possibility shown in Fig. 5.

Pathologic Report (Summary).—The gall bladder showed adhesions and two openings, one labeled "hepatic duct" measuring 0.7 cm. and the other labeled "common duct" measuring 0.3 cm. The wall was thick and tough and the contents consisted of numerous faceted calculi which were irregular in shape and were imbedded in soft friable material.

Microscopic examination showed the mucosa to be infiltrated with chronic inflammatory cells and the subjacent tissue to be edematous and densely fibrous.

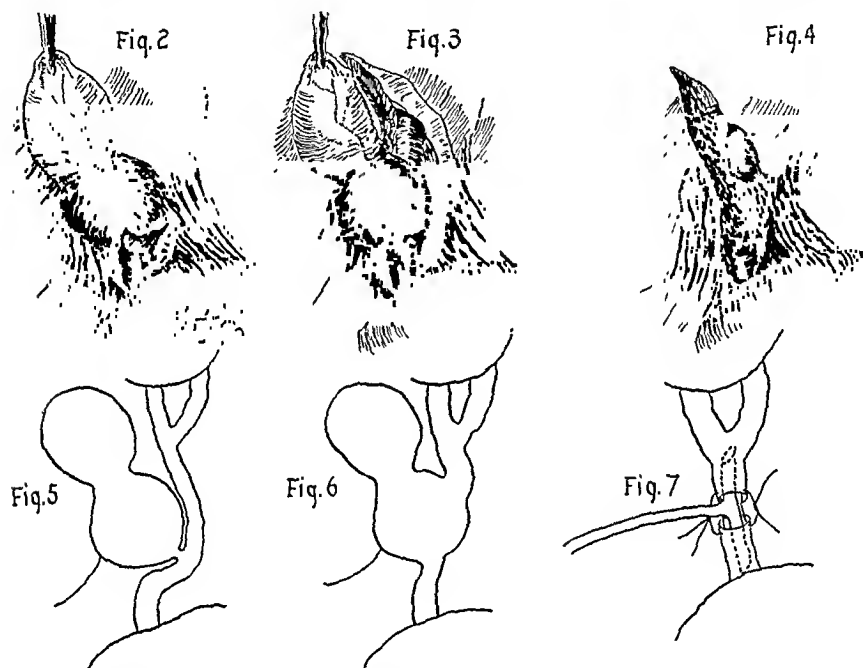


Fig. 2.—Shows duct leaving lower segment of gall bladder and passing down behind duodenum.

Fig. 3.—Shows second duct entering lower pouch of gall bladder from above.

Fig. 4.—Shows ends of divided ducts as seen after removing gall bladder.

Fig. 5.—Condition which had to be excluded, i.e., a short or absent cystic duct with the common duct closely adherent to the gall bladder.

Fig. 6.—Shows the arrangement actually present in this case.

Fig. 7.—Shows the duct ends being anastomosed over a T tube.

Discussion.—The unusual condition described presents many interesting points in connection with operative technique and possible etiology.

During the operation one's chief concern is to exclude the condition shown in Fig. 5, where with a very short cystic duct the neck of the gall bladder is densely adherent to the common duct. With the gall bladder opened and the orifices of the ducts visualized and demon-

strated by the passage of a probe into them, the true situation was clearly apparent. This demonstrates the value of opening the gall bladder during operation in certain puzzling cases.

The question of etiology of the condition reported is also of considerable interest. Several surgeons of extensive experience, with whom this case has been discussed, suggest that the condition was an acquired one.

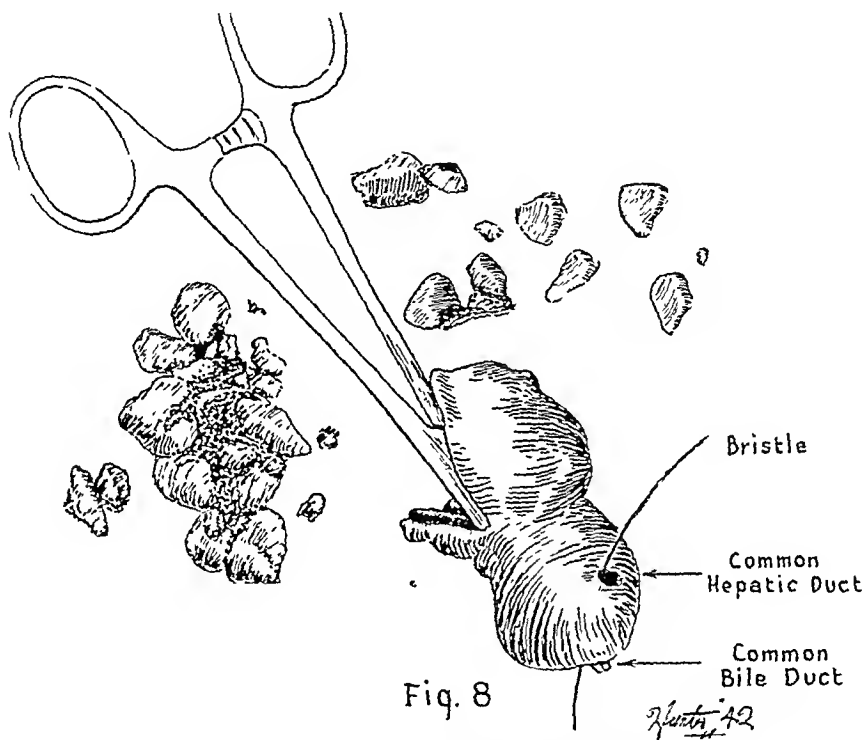


Fig. 8.—Shows specimen after removal with a bristle passing through the two duct openings and the tip of a forcep protruding through the lower or common duct opening.

In the presence of a short cystic duct, such as all surgeons have encountered at operation, it is possible that a stone in the duct might progressively enlarge causing a gradual dilation of the cystic duct as well as the adjacent common duct and neck of the gall bladder as shown in Fig. 12, *a* and *b*. The lower pouch of the "gall bladder" would then consist largely of dilated cystic duct. The fact that it lay entirely within the folds of the hepatoduodenal ligament lends color to this view as does the large mass of stones which was present.

The condition found in this case may also be explained on the basis of a congenital anomaly. One condition which must be considered is diverticulum of the common bile duct. Walton¹ has reported six per-

sonal cases and refers to between eighty and ninety similar cases reported by various authors. In his cases and those to which he referred, the gall bladder was present in its normal form and position but there was a large cystic pouch projecting from the lower portion of the common bile duct. This pouch was eccentric and projected to the right and extended above and behind the duodenum. The diverticulum resembled a saccular rather than a fusiform dilatation. This is

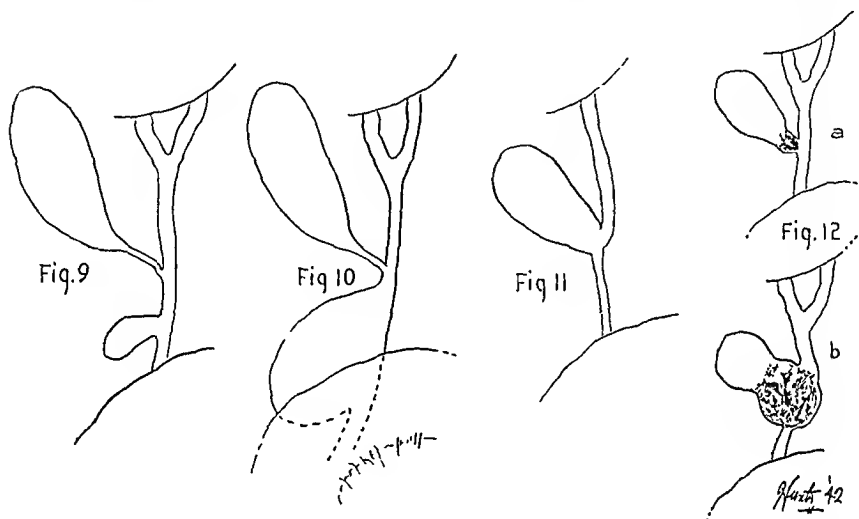


Fig. 9.—Illustrates a congenital anomaly as reported by Wolfson, i.e., a rudimentary gall bladder with a diverticulum of the common duct.

Fig. 10.—Shows the usual type of congenital diverticulum of the common duct associated with gall bladder of normal size and position.

Fig. 11.—Illustrates the type of anomaly caused by the absence of the common duct where the cystic duct enters the duodenum directly.

Fig. 12.—Illustrates a possible acquired origin of the condition found in this case.

probably the condition actually present in those cases reported in the literature as "Congenital Cystic Dilatation of the Common Bile Duct." Walton states that the opening of the common hepatic duct in the upper part of the sac was directly opposite that of the common bile duct below. They lay on the medial aspect of the pouch and were connected by a shallow groove. This suggested that only the lateral wall of the common duct was involved in the protrusion. He assumed that some congenital weakness existed in this part of the duct wall allowing it to protrude gradually as a saccular pouch (Fig. 10).

Wolfson² also reports a similar case in which there was a rudimentary gall bladder in the normal situation and a diverticulum of the common duct lower down containing calculi as shown in Fig. 9.

To make this explanation fit the case in point one would have to assume one of the two following conditions: (1) The occurrence of a diverticulum at the site of the cystic duct and represented in this case

by the lower pouch of the structure removed, the upper pouch being the true gall bladder; (2) the congenital absence of the normal gall bladder and the development of a diverticulum which represented the entire structure removed in this case.

Because the structure occupied the normal situation of the gall bladder and was attached to the under surface of the liver as usual, I am inclined to reject the explanation that it represents a congenital diverticulum.

The simplest and most logical explanation of the anomaly encountered in the case reported is an anomaly of the ducts, probably the congenital absence of the cystic duct. The hepatic duct entered the gall bladder from above and the common bile duct took exit from its lower aspect, the gall bladder forming the only connection between them. Walton³ has reported a case of this type. Mentzner⁴ points out that the cystic duct is very short in many cases and states that nine cases of true congenital absence of the cystic duct have been reported. All surgeons of experience have, of course, encountered the very short cystic duct at operation. Mentzner states further that in certain animals it is very short and is absent in the badger and baboon. He also makes the interesting statement that the anomalies found in man represent a reversion to the normal arrangement in certain animals. Mentzner also points out that the common duct is absent in some animals, the hepatic duct entering the gall bladder from above and the cystic duct entering the duodenum below. The cystic duct in these cases replaces the common duct (Fig. 11). Whether the duct connecting the gall bladder with the intestine is embryologically the cystic or the common duct, in the case recorded, one cannot say. Either anomaly, namely, the absence of the cystic duct or the absence of the common duct, would appear to adequately explain the condition found in this case. Of course, the large mass of stones found in the lower segment of the gall bladder representing Hartmann's pouch would cause distension of this segment with occlusion of the hepatic duct and production of the jaundice present in this case.

CONCLUSION

1. An unusual anomaly of the bile ducts is described and its possible etiology as a congenital or acquired condition is discussed.
2. The case presented considerable diagnostic interest because of the entire absence of pain in the presence of obstructive jaundice due to gallstones.
3. The technical difficulties are described and the following practical conclusions may be drawn:
 - (a) In every case of surgery upon the biliary tract thorough exposure of the hepatic, common, and cystic ducts is essential.

sonal cases and refers to between eighty and ninety similar cases reported by various authors. In his cases and those to which he referred, the gall bladder was present in its normal form and position but there was a large cystic pouch projecting from the lower portion of the common bile duct. This pouch was eccentric and projected to the right and extended above and behind the duodenum. The diverticulum resembled a saecular rather than a fusiform dilatation. This is

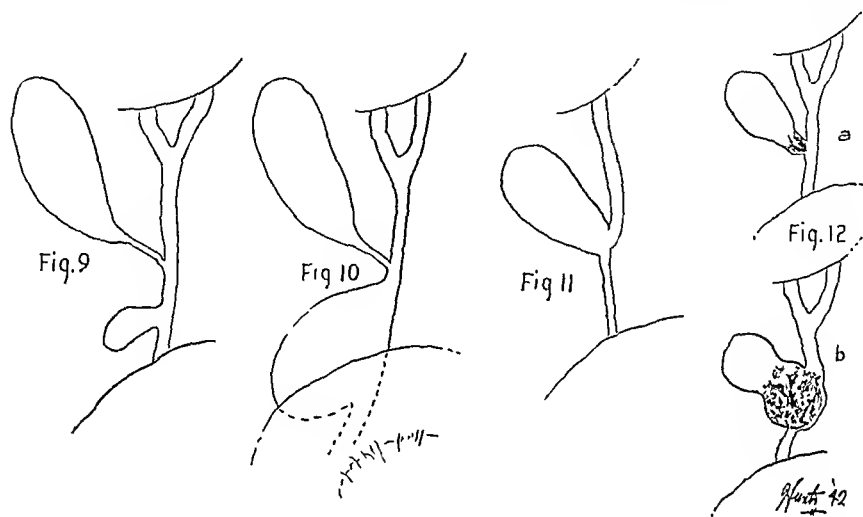


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THE TREATMENT OF COMMON DUCT STONE MISSED AT OPERATION

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TO LEAVE a stone in the common or hepatic bile ducts during surgery on these structures is not a rare occurrence. Surgeons admit freely the high incidence of stones left in the biliary tree following surgery directed for their removal. The embarrassing facts associated with this situation are a continuance of the patient's symptoms of dyspepsia, pain, jaundice, chills and fever, and the high mortality rate associated with a secondary search for these stones. These secondary operations are so undesirable that any less difficult or hazardous procedure of dealing with the overlooked common duct stone is very acceptable.

The practice of using cholangiography at operation, as advocated by Mirizzi,¹ or postoperatively before removal of the T tube in the common bile duct,² has enabled the surgeon to determine quite accurately the presence or absence of obstruction to the outflow of bile from the biliary ducts.

By combining cholangiography and a study of varying pressure within the common bile duct under varying conditions, Walters and his associates made some very valuable findings on the physiology and pathologic physiology of the common bile duct,³ together with the pharmacologic action of various drugs on this duct and the sphincter of Oddi.⁴

Pribram,⁵ in 1935, reported the dissolution of stones in the common duct by the injection of ethyl ether through a drainage tube in the duct.

Walters and Wesson⁶ report a case in which a common duct stone was caused to fragment by three daily injections of 5 c.c. of ethyl ether, and with two additional injections of one-third ethyl alcohol and two-thirds ether it passed into the duodenum with the aid of amyl nitrite inhalations as a relaxant to the sphincter of Oddi.

REPORT OF CASES

CASE 1—Mrs. D., aged 33 years, entered the hospital, June 6, 1937, because of marked jaundice. Her present trouble began suddenly four weeks previously, with severe pain under the right costal arch, radiating into the subscapular area. Morphine administered hypodermically was required to control the pain, which lasted a few days and suddenly subsided. The temperature rose to 101° F. near the onset and gradually returned to normal. Definite jaundice was in evidence after two or three days and gradually increased to the time of admission.

The patient had a cesarean section five months previously. Her convalescence was complicated by thrombophlebitis and multiple pulmonary infarcts. A second incidence of thrombophlebitis caused her to remain in bed until about six weeks prior to this admission.

(b) If this is observed radical surgery may be safely carried out even in the presence of the most anomalous conditions.

(c) The value of opening the gall bladder in certain complicated cases for the purpose of exploration from within its cavity is emphasized.

REFERENCES

1. Walton, Sir James: Congenital Diverticulum of the Common Bile-Duct, Brit. J. Surg. 27: 295, 1939.
2. Wolfson, W. L.: Supernumery Gall Bladder, Am. J. Surg. 6: 88, 1939.
3. Walton, Sir James: Congenital Abnormalities, Brit. J. Surg. 9: 169, 1921; also The Surgical Dyspepsias, London, 1923, Edward Arnold & Co., p. 451.
4. Mentzer, S. H.: Anomalous Bile Ducts in Man, J. A. M. A. 93: 1273, 1929.

Convalescence was quite satisfactory until the sixth postoperative day, when there was very free bleeding in the wound and around the drainage tube. Red blood count dropped to 1,440,000 and the hemoglobin to 37 per cent. Small daily transfusions were being given. After forty eight hours the bleeding stopped temporarily and the red blood count and hemoglobin rose to 3,220,000 and 65 per cent respectively. On the fourteenth postoperative day there was further bleeding and the red blood count dropped to 2,760,000 and the hemoglobin to 53 per cent. At this time there had been very little bile from the T tube and little or no decrease in the jaundice. About the twentieth postoperative day the jaundice began to decrease, the bleeding ceased, and an increased amount of bile drained from the T tube. Special laboratory tests requiring vena puncture were omitted because of the inaccessibility of the veins and therefore the serum bilirubin levels were not known. Intravenous solutions and transfusions were given by continuous drip through a cannula tied in the vein. Subsequent progress was very satisfactory.



Fig 1B—Cholangiogram of Case 1 after dissolution of the common duct stone by the ether-alcohol mixture before removal of T tube

On the thirty fourth postoperative day a cholangiogram was made by injecting lipiodol through the T tube. A shadow interpreted as a stone was seen in the distal end of the common duct (Fig 1A).

A mixture of one third ethyl alcohol and two thirds ethyl ether in amounts of 5 cc was injected daily into the T tube, for five days.

The following day a cholangiogram failed to show any evidence of stone (Fig. 1B). A subsequent cholangiographic study after three days revealed a prompt and free flow of the injected media into the duodenum. After the latter study the T tube was removed. The patient has remained well to date.

Family history seemed irrelevant.

Examination.—The patient was obese, weighing 200 pounds. On admission the temperature was 98.4° F., pulse 84, and blood pressure 84/50. Skin and sclera were a deep yellow color. General physical examination was otherwise essentially negative. No definite tenderness, spasticity, or sense of mass could be made out in any part of the abdomen.

Bile graded 3+ was reported on urinalysis but only a faint trace was found in the stool. The urine, which had a specific gravity of 1.010, contained albumin 1+.

The white blood count was 5,800, the red blood count was 4,940,000, and the hemoglobin was 94 per cent.

The coagulation time was six minutes and the bleeding time was three minutes and forty-five seconds.*



Fig. 1A.—Postoperative cholangiogram of Case 1 showing shadow of stone in ampulla of Vater.

A diagnosis of obstructive jaundice was made and the patient prepared for surgery by intravenous solution of glucose, calcium gluconate, and small blood transfusions.

At operation, June 9, 1937, the common bile duct was found to be about 1 cm. in diameter. The common duct was opened and a probe passed easily into the duodenum and up either hepatic duct. The head of the pancreas seemed slightly enlarged. Prolonged exploration of the bile ducts failed to reveal evidence of obstruction. The liver was very dark in color and showed diffuse hepatitis grade 1+. The gall bladder was about normal size and showed moderate thickening. The gall bladder was removed and a T tube was placed in the common duct. The gall bladder showed mild chronic inflammatory changes and contained 3 to 4 c.c. of thick black bile.

*The prothrombin time was not in general use at this time.

A diagnosis of acute cholecystitis and cholangitis was made. The high fever and leucocytosis were highly suggestive of a gangrenous condition of the gall bladder but the patient seemed desperately ill and in a state of mild shock, so that surgery was deferred and supportive measures instituted. Ten per cent glucose in saline solution with thiamin chloride was given intravenously in amounts of 3,000 c.c. in twenty-four hours. Sweetened fruit juices were offered per os as tolerated.

An injection of 1 c.c. of synthetic vitamin K was administered intramuscularly. The patient was typed for transfusion and repeated white blood counts were ordered. The temperature rose rapidly to 105° F. and then receded. After eighteen hours the temperature and white blood count were markedly lower. Sulfathiazole therapy was instituted and after eight days the septic course had definitely subsided. Bile appeared in the stools at this time. The blood pressure was 120/80, pulse 96, and temperature 99 to 100° F. The white blood count was 15,000 and the prothrombin time was normal. A total period of twelve days was used for preoperative preparation. Intravenous fluids and glucose were gradually replaced by oral fluids, a high carbohydrate, high protein, low fat diet with supplemental high vitamin intake.

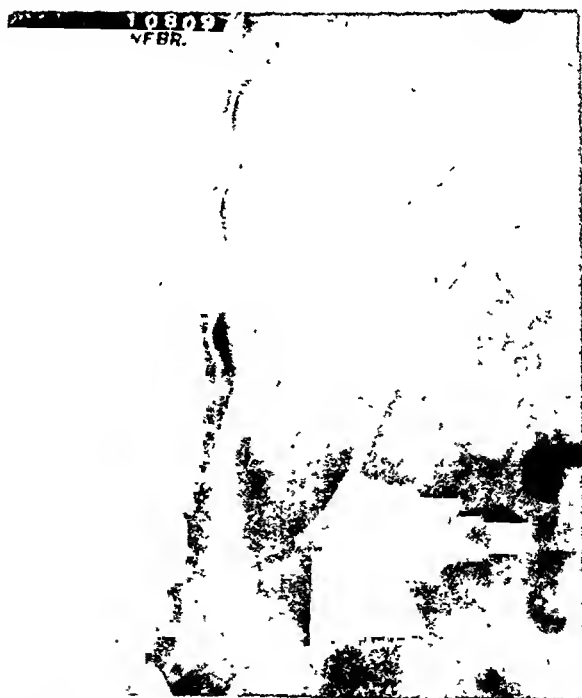


Fig. 2B—Cholangiogram in Case 2 showing prompt passage of opaque media from common duct into the duodenum after the ether-alcohol injections.

At operation on the twelfth hospital day the gall bladder was found to be small, markedly thickened, and injected with a small gangrenous area at the fundus, which was adherent to the abdominal wall. It was filled with stones of various sizes. The great omentum was adherent to the gall bladder and bile ducts. The common bile duct was markedly dilated, surrounded by edematous tissue, and contained several large stones. The liver showed diffuse hepatitis grade 1.

The common duct was opened, the stones removed by scoop, and the common and hepatic ducts explored and flushed out with saline solution. The probes, scoops,

CASE 2.—Mrs. B., aged 37 years, entered the hospital, Aug. 19, 1941, because of severe right upper quadrant pain, jaundice, chills and fever. The present trouble began five days prior to admission, as a sudden, severe, sharp pain under the right costal arch, radiating to the tip of the right scapula. Two days later a yellow tint to the skin and sclera developed and gradually deepened. This was accompanied by chills and fever. Repeated hypodermic injections of morphine sulfate were required to control the pain.

In the past history was a story of a gall bladder type of dyspepsia of ten years' duration, with recurrent mild attacks of right upper quadrant distress.

The patient's father died at the age of 46 years from cancer of the colon. Family and personal history were otherwise essentially negative.

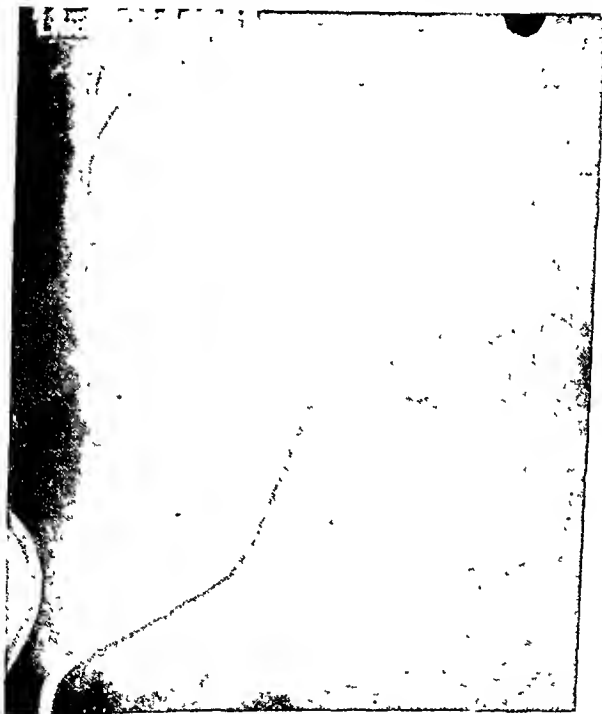


Fig. 2A.—Postoperative cholangiogram in Case 2 showing stone or stones impacted in the ampulla of Vater.

Examination revealed an obese female apparently very ill, with a temperature of 102° F., a pulse count of 142, and a blood pressure of 90/60. Other positive findings were a deep icteric tint of the skin and sclera, marked tachycardia, and moderate tenderness over the gall bladder, which was palpable below the costal margin.

Urinalysis of a catheterized urine specimen showed: Specific gravity 1.010; pH, 5.5; albumin, ++; bile, ++; pus and granular casts, +. The white blood count was 37,450 and the hemoglobin was 82 per cent. A Schilling hemogram showed a marked shift to the left. The prothrombin time was one minute and fifteen seconds (normal is twenty-three seconds). The van den Bergh test gave an immediate direct response with a value of 14.2 mg. per cent for serum bilirubin.

An electrocardiographic study was interpreted as showing a toxic myocardiosis.

COMMENT

It has become common practice to explore and place some type of drainage tube in the common bile duct in cases of suspected or apparent stone or other obstructive pathology.

Employment of postoperative cholangiography permits the surgeon to evaluate the results of his operative efforts and discover any residual stone or other obstruction before the drain is removed. Attention should be called to the fact that a single cholangiogram may show obstruction which is the result of local spasm and be erroneously interpreted as organic obstruction. The value of taking a series of cholangiograms in one such case is shown in Figs. 3A and 3B.



Fig 3B—Cholangiogram of same case as Fig. 3A, taken a few minutes later and proving the fallacy of relying on a single cholangiogram.

The majority of gallstones show a high content of cholesterol, which dissolves or disintegrates readily by ether. This fact has been utilized to dissolve common duct stones missed at operation. This procedure has been successful in the cases here reported and is certainly preferable to a secondary operation.

Best and Hicken¹ have utilized the findings of other workers on the antispasmodic action of certain drugs on the sphincter of Oddi and the choloretic action of various substances together with bile duct irrigations in developing their "biliary flush." This is no doubt an excellent

and irrigating solution passed freely and easily into the duodenum. A T tube was placed in the common duct. A subtotal cholecystectomy as advocated by Estes⁷ was carried out and a tube inserted into the stump of the cystic duct.

In the first forty-eight-hour postoperative period the patient developed marked hyperpyrexia and an area of atelectasis in the lower lobe of the right lung posteriorly. The Trendelenburg position, carbon dioxide inhalations, and frequent change of posture were thought to contribute to a prompt disappearance of these complications. Bile began draining promptly and in good amount from both drainage tubes. The wound healed promptly and firmly.

An attempt to clamp the cystic duct and common duct tubes on the twelfth postoperative day produced epigastric distress, nausea and vomiting, and moderate fever. The tubes were permitted to drain and sulfathiazole was administered. Four days later this drug was discontinued because of a dermatitis.

Cholangiograms on the sixteenth and twenty-sixth days postoperatively revealed an obstruction in the common duct interpreted as a stone, or stones, in the ampulla of Vater (Fig. 2A).



Fig. 3A.—A postoperative cholangiogram showing a filling defect which might be erroneously interpreted as a stone

Six daily injections of a mixture of 4 c.c. of ether and 2 c.c. of ethyl alcohol into the T tube were given. After the fourth injection the stools, which had varied from clay color to light brown, became dark brown, and the epigastric distress disappeared. It was now possible to keep the T tube clamped constantly. The tube in the cystic duct had been removed and the second cholangiogram showed this tract to be closed. Cholangiograms on the day following the last instillation of the ether-alcohol mixture demonstrated a prompt and free discharge of the media from the common duct and failed to demonstrate any shadow of stone or other obstruction (Fig. 2B).

THE EFFECT OF ANESTHETICS ON GASTRIC TONUS AND MOTILITY WITH SPECIAL REFERENCE TO ACUTE GASTRIC DILATATION*

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IT IS generally agreed that in acute dilatation of the stomach there is a loss of gastric muscle tonus with the result that accumulated secretions and gas can balloon out the relaxed viscus.^{4, 6, 11, 12, 13, 15, 39} There is regurgitation of variable amounts of fluid. Dehydration, symptoms of toxemia, and collapse are features of the condition if it is progressive and unrelieved.

It seems clear from the work of Dragstedt and others¹³ that, once the stomach has become dilated, the main factor in the pathogenesis of the condition is the failure of the gastric and pancreatic juices to be reabsorbed. These secretions stagnate in the atonic stomach or are lost by regurgitation, and fail to reach the lower absorbing portion of the gastrointestinal tract. Water and the inorganic elements, sodium and chloride, are lost from the blood plasma. Dehydration and alkalosis result and, unless the fluid and electrolytic balance is re-established, death results.

The problem then seems to be: Why does the stomach become atonic in the first place and in some cases remain so for a considerable length of time, even in spite of treatment? Clinically, acute gastric dilatation has been observed in association with a wide variety of conditions, among which may be mentioned its occurrence following an attack of migraine,²⁰ during the course of pulmonary tuberculosis,³⁴ in severe diabetes,¹ and following various operative procedures.¹³ There are, undoubtedly, multiple etiologic factors. In the majority of cases, however, the condition has occurred postoperatively, and in these cases it has occurred most frequently following laparotomy among patients who have had a general anesthetic. It has been only natural to look to the effects on the stomach incident to operation, either the operative procedure itself or the anesthetic or both, in seeking an explanation of this complication.

Dragstedt¹² reviewed the question of the causation of acute postoperative gastric dilatation and concluded that the primary cause for the reduction of gastric tonus is an inhibition caused by reflex stimulation of vagus and splanchnic nerves to the stomach during the course of the operation. This author noted, however, that no amount of stimulation

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procedure to overcome obstruction from spasm, inspissated bile, or very small stones but it does not seem feasible for the larger stones such as were demonstrated by the x-ray in the cases here reported. Best⁹ has recently reported this limitation in the use of his nonoperative regime.

SUMMARY

Two cases of common bile duct calculus are reported in which stones remained in the duct after operation. In each case the stone was disintegrated by the action of ether and alcohol injected into the T tube. This dissolution of the stone and its passage into the duodenum were demonstrated by cholangiographic studies.

REFERENCES

1. Mirizzi, P. L.: Operative Cholangiography, *Surg., Gynec. & Obst.* 65: 702-710, 1937.
2. Walters, Waltman, and Thiessen, N. W.: Visual Methods of Studying the Physiology of the Bile Ducts. I. The Problem of Pancreatitis and Sphincteritis, *Proc. Staff Meet., Mayo Clin.* 9: 772-775, 1934.
3. Walters, Waltman: The Pathological Physiology of Stone in the Common Bile Duct: Clinical and Surgical Significance, *Surg., Gynec. & Obst.* 63: 417-424, 1936.
4. Butsch, W. L., McGown, J. M., and Walters, Waltman: Pressure in the Common Bile Duct: A Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 11: 145-150, 1936.
5. Pribram, B. O.: New Methods in Gallstone Surgery, *Surg., Gynec. & Obst.* 60: 55-64, 1935.
6. Walters, Waltman, and Wesson, H. R.: Fragmentation and Expulsion of a Common Duct Stone Into the Duodenum, Using Ether and Amyl Nitrite: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 12: 260-262, 1937.
7. Estes, W. L., Jr.: Partial Cholecystectomy, *Arch. Surg.* 36: 849-857, 1938.
8. Best, R. Russell, and Hicken, N. Frederick: Nonoperative Management of Remaining Common Duct Stones, *J. A. M. A.* 110: 1257-1261, 1938.
9. Best, R. Russell: The Acute Gall Bladder, *Surg., Gynec. & Obst.* 73: 219-312, 1941.

of the newer agents and combinations of agents, on the gastric tonus and motility of the dog under the following conditions: (1) in animals in which the extrinsic gastric nerves were present; (2) after bilateral splanchnicectomy and double vagotomy; (3) after bilateral splanchnicectomy only; and (4) after double vagotomy only.

METHOD

The effects of anesthetics on the motor activity of the stomach were studied in dogs that had permanent gastric fistulas. Young healthy dogs weighing 7 to 16 kg. were selected and trained to lie quietly on the right side. The Mann-Bollman type of fistula was employed (Fig. 1). This was prepared by a two-stage procedure. In the first stage a loop

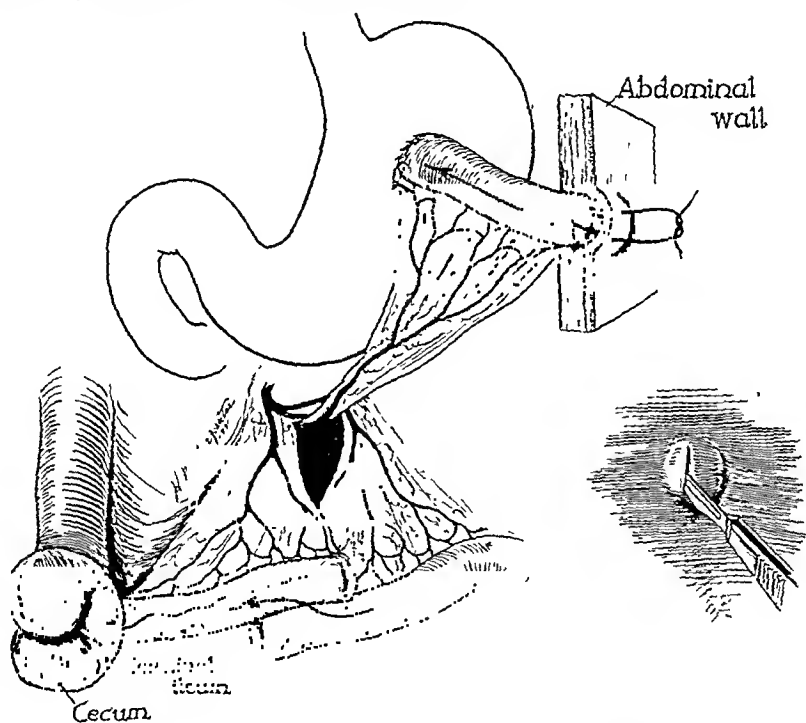


Fig. 1.—Mann-Bollman fistula; distal (aboral) end of isolated loop of terminal ileum anastomosed to stomach, proximal (oral) end closed and anchored in subcutaneous position, continuity of ileum established; direction of peristaltic activity indicated by arrows; closed loop of ileum converted into a fistula by opening it through a short skin incision.

of the terminal portion of the ileum 8 to 10 cm. in length was isolated. The continuity of the ileum was established by a side-to-side anastomosis. The distal (aboral) end of the loop was anastomosed to the stomach near the middle of the corpus; the proximal (oral) end was closed, passed through a stab wound in the upper portion of the left rectus muscle, and anchored in a subcutaneous position. The abdomen was closed in layers. The proximal end of the loop was closed and left beneath the

of these nerves in the experimental animal would produce the condition and he concluded that, in addition, the gastric musculature must be depressed by the anesthetic in order for the symptom complex to be produced. It is with the role of anesthesia as a possible etiologic factor that the present investigation is concerned.

Kelling found that he could produce an enormous degree of gastric distention in dogs by pumping in air through a gastrotomy opening if the animals were first anesthetized. In unanesthetized dogs he could produce only a moderate degree of distention because regurgitation through the esophagus emptied the stomach as soon as the intragastric pressure rose.

Báron and Bársony carried out roentgenoscopic studies on the gastrointestinal tract of dogs during anesthesia with chloroform and ether. They observed marked relaxation of the stomach with both these agents. Peristalsis was abolished. In some cases full relaxation persisted for one hour after discontinuance of the anesthetic and recovery was complete only after three or four hours.

Miller, using the balloon-recording method, studied the effects of general anesthesia on the muscular activity of the gastrointestinal tract of dogs that had permanent fistulas. This investigator observed a decrease in gastric tonus and a reduction in motility during third stage anesthesia with ether and chloroform. In some instances the stomach was still somewhat depressed as long as five hours after recovery of consciousness. With nitrous oxide, after administration of the anesthetic had been discontinued, there were a decrease of tonus and a reduction in motility similar to those which occurred with ether anesthesia.

Bisgard and Johnson found gastric tonus and motility to be depressed by ether and nitrous oxide in both man and dog. On the other hand, these workers found that with some agents, notably cyclopropane-oxygen alone, and especially cyclopropane-oxygen as a supplement to a basal anesthetic of avertin with amylene hydrate, gastric activity was increased. They suggested that this difference in action might be dependent on the relative quantity of oxygen in the blood and tissues during anesthesia. Another explanation which has been offered concerning the difference in action observed with different anesthetics is that the effects of some agents might be mediated through the sympathetic nervous system and other agents might affect the gastric musculature directly.⁷

The effect of anesthesia on gastric tonus and motility is of further interest in view of the ever-increasing use of newer and special anesthetic agents which are employed alone or in combination with other agents. The trend toward the more frequent use of the newer agents may be seen from the periodic clinical reports on anesthesia such as those of Lundy and his associates.²³

In order to evaluate more properly the question of anesthesia as a possible etiologic factor in acute gastric dilatation, it was decided to make a comparative study of the effects of an

An attempt was made to determine the position of the balloon in the stomach roentgenographically. This was not entirely satisfactory. In order to outline the walls of the stomach accurately in relation to the balloon it was necessary to introduce a considerable amount of contrast medium into the stomach. This represented the position of the balloon in a partially filled stomach and did not meet the conditions of this investigation. Accordingly, when all experiments were completed, laparotomy was performed on three fasted dogs and the position of the balloon was determined by inspection, after which the dogs were killed. Laparotomy was performed under pentothal sodium anesthesia. In all instances the stomach was found contracted on the balloon which occupied the proximal portion of the prepyloric region, all of the corpus, and most of the fundus, as was determined by palpation and verified by direct inspection after the stomach had been opened.

Observations of the effects of anesthetics on gastric tonus and motility were repeated after splanchnicectomy and vagotomy. For this denervation a two-stage procedure was employed. The first stage consisted of a thoracic approach through the eighth interspace on the left side. Segments measuring 2 cm. in length were removed from each of the vagal trunks as they lie on either side of the esophagus immediately above the esophageal hiatus of the diaphragm. In this location the trunks have been formed from the pulmonary plexus but have not yet divided into the various rami which supply the stomach and other abdominal viscera. The lower seven sympathetic ganglia and connecting chain, as well as the emergent splanchnic nerves in practically their entire extent, were removed. When recovery was complete, usually after two to three weeks, splanchnicectomy was performed through the eighth interspace on the right side in a manner identical with that employed on the left. Bilateral splanchnicectomy and double vagotomy were performed on four dogs by this two-stage procedure.

Trausthoracic double vagotomy only was done on two dogs and bilateral splanchnicectomy only was performed on two dogs by the procedures herein described. All dogs on which double vagotomy was performed vomited for a few days after the operation. This occurred shortly after feeding but not all the food ingested was lost by vomiting. Ultimately the vomiting ceased altogether and the dogs appeared perfectly normal. There was no vomiting in the dogs submitted to bilateral splanchnicectomy only.

RESULTS

A. Effects of Anesthetics on Gastric Tonus and Motility in Animals in Which the Extrinsic Gastric Nerves Are Intact.

1. *Ether* (Fig. 2a).—The effect of ether anesthesia on gastric tonus and motility was studied in twelve dogs. Induction of anesthesia was carried out by the open drop method. Anesthesia was carried to plane

skin to protect the gastroenteric anastomosis from bacterial contamination from the skin surface. Two weeks after the first procedure the closed loop of ileum was converted into a fistula by opening it through a short incision in the skin and suturing the edges to the margin of the skin. By giving the loop this relation with respect to the stomach and the abdominal wall, peristaltic activity is directed toward the former and away from the latter. In no instance was there leakage of gastric contents on the skin of the abdominal wall. The dogs appeared perfectly normal after establishment of these fistulas, and the latter were still functioning well at the time of necropsy, which was in some instances as long as thirteen months after the fistulas had been established.

The apparatus used to record the motor activity of the stomach was the balloon-bromoform manometer apparatus similar to that described by Carlson. A deflated condom balloon attached to the end of a No. 20 French hard rubber catheter was passed through the fistula into the stomach. The other end of the catheter was attached to a rubber tube connected with the manometer. One hundred and eighty cubic centimeters of air were introduced into the balloon; this amounted to a pressure of 2 to 6 cm. bromoform. The volume was not sufficient to stretch the walls of the balloon. A writing lever attached to a float riding on the column of bromoform recorded the activity of the stomach on a slowly revolving kymograph. Because this method records changes of diaphragmatic pressure, a concomitant record of the respiratory excursions was made by a standard pneumographic method.

The tracings obtained by this technique show contractions and alterations in tone of the gastric musculature. The latter are represented by changes in the level of the "diastolic" line of the tracing.

The animals were fasted for eighteen to twenty-four hours preceding each experiment. A control observation of fifteen to thirty minutes was made before each anesthetic was given. The most frequently observed type of contractions during the control period was type II, according to the criteria of Carlson. In this type of contractions the tonus of the stomach is relatively high and the contractions follow one another in rapid succession. The duration of the contractions varies between twenty and thirty seconds. The contractions may vary to some extent in amplitude and rate, but otherwise are practically continuous.

Observations were not made during the periods of induction of, nor reactions from, the anesthetics because during these periods exaggerated respiratory excursions and bodily movements made recording of gastric motor activity impossible. Observations were made at various intervals after administration of the anesthetics had been discontinued until gastric tonus and motility had returned to the control level.

The anesthetic gases were administered by means of an apparatus which allows rebreathing of the gases and which was designed by Mousel and Seldon for use on laboratory animals. Carbon dioxide was absorbed from the exhaled gases by means of soda lime. This apparatus was attached to a standard clinical gas machine.

2. *Ether With Premedication of Morphine and Atropine* (Fig. 2b).—Observations were made on six dogs. Morphine sulfate in doses of 0.5 to 0.75 mg. per kilogram of body weight and atropine sulfate in a dose of 0.023 mg. per kilogram of body weight were given hypodermically. Morphine in this dosage produced a state of drowsiness in the dog which was thought comparable to that produced in man after the usual pre-operative administration of morphine.

In all observations after the administration of morphine there was a transient increase in gastric tonus and motility followed by a marked decrease in motility and a moderate reduction in tonus. There was little further effect on gastric activity after the administration of atropine. After etherization to the third stage there were a further decrease in tonus and complete loss of motility. The average time required for tonus and motility to return to normal was five hours and fifteen minutes.

3. *Nitrous Oxide-Oxygen and Ether*.—Observations were made on six dogs. For these experiments an ether vaporizer was attached to the gas machine. With nitrous oxide-oxygen the animals were anesthetized as deeply as possible without producing cyanosis. Ether was then added and the degree of anesthesia was carried as nearly as possible to plane 2 of the third stage and held there for fifteen minutes. Very little skeletal muscular relaxation was produced by the gas-oxygen alone and during this period gastric motor activity was unaffected. After ether was added and anesthesia carried to the third stage, there was marked reduction in gastric tonus and motility was entirely abolished. The time required for tonus and motility to return to normal fell within the range of that required for ether alone.

4. *Ether Supplemental to a Basal Anesthetic of Avertin With Amylene Hydrate* (Fig. 2c).—Observations were made on five dogs. Avertin with amylene hydrate in a dose of 100 mg. per kilogram of body weight was administered thirty minutes before ether was given. With avertin, gastric motor activity was unaffected in three dogs. In two dogs the amplitude of contractions was moderately reduced. In all instances, after anesthesia was carried to the third stage with ether, the effect on gastric tonus and motility was the same as with ether alone.

5. *Prolonged Ether Anesthesia*.—The effect of prolonging ether anesthesia on gastric motor activity was studied in five dogs. Third stage ether anesthesia was maintained for one hour and fifteen minutes. The results were very similar to those obtained with the fifteen-minute period of ether anesthesia. The time required for tonus and motility to return to normal averaged ten minutes longer than that required when ether anesthesia was maintained for only fifteen minutes.

6. *Cyclopropane-Oxygen* (Fig. 2d).—The effect of cyclopropane-oxygen anesthesia on gastric motor activity was studied in seven dogs. Anesthesia was carried to plane 2 of the third stage and maintained at the level for fifteen minutes. Skeletal muscular relaxation was thought to

2 of the third stage, according to the criteria of Guedel, and maintained as nearly as possible at the level for fifteen minutes. In every instance gastric tonus was greatly diminished and motility completely abolished. The time required for tonus and motility to return to normal was from one hour and fifteen minutes to ten hours. In eight dogs the motor activity had returned to normal two to three hours after the anesthetic was discontinued. Usually tonus began to return before motility; otherwise tonus and motility returned together.

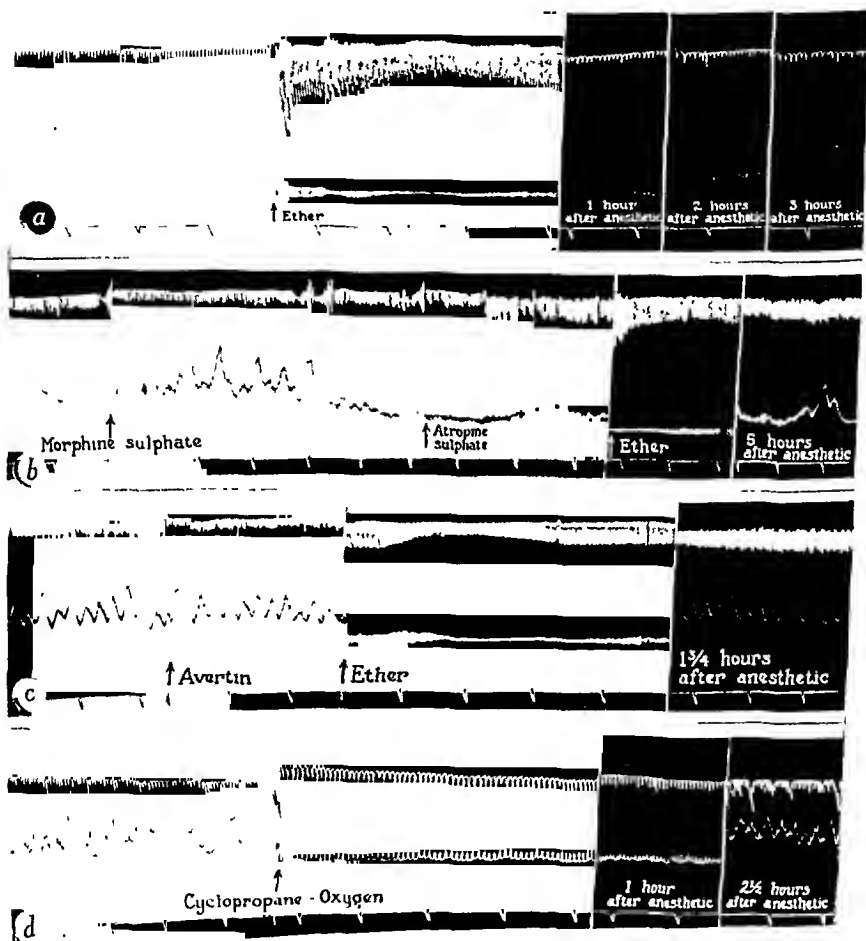


Fig. 2.—Effect of anesthesia on gastric contractions. *a*, Ether anesthesia, Dog 11 (weight 11 kg.). Upper tracing in this and subsequent figures shows respiratory excursions; middle tracing shows gastric contractions and superimposed diaphragmatic pressure changes; third stage anesthesia indicated by arrow; time interval in this and subsequent figures one minute.

b, Ether anesthesia with premedication of morphine and atropine, Dog 7 (weight 15.5 kg.). Morphine sulfate, 7.75 mg., and atropine sulfate, 0.3 mg., given hypodermically; third stage ether anesthesia indicated by arrow.

c, Ether supplemental to a basal anesthetic of avertin, Dog 11 (weight 11 kg.). First arrow thirty minutes after avertin in amylene hydrate, 1.1 c.c. in 44 c.c. water, given by rectum; third stage anesthesia indicated by second arrow.

d, Cyclopropane-oxygen anesthesia, Dog 1 (weight 9 kg.). Third stage anesthesia indicated by arrow.

anesthesia with nitrogen-oxygen in a 3 to 1 ratio was produced without cyanosis.

5. *Third Stage Anesthesia*.—Observations were made on eight dogs. Anesthesia carried to the third stage was produced with nitrogen-oxygen without cyanosis. There was a moderate decrease in tonus and a complete abolition of motility. In these instances there was very little skeletal muscular relaxation.

A depth of anesthesia sufficient to produce skeletal muscular relaxation was always accompanied by cyanosis. In these observations the effects on gastric tonus and motility were very similar to those obtained with ether.

9. *Ethylene-Oxygen*.—The effect of ethylene-oxygen on gastric motor activity was studied in seven dogs. In four dogs, third stage anesthesia with moderate skeletal muscular relaxation was produced, unaccompanied by cyanosis. There was a moderate decrease in tonus and a complete abolition of motility in these instances. The average time required for tonus and motility to return to normal was one hour.

In three dogs a depth of anesthesia sufficient to cause skeletal muscular relaxation could not be obtained without producing cyanosis. In these observations there was little effect on gastric tonus and motility.

10. *Intravenous Pentothal Sodium* (Fig. 3a).—Observations were made on seven dogs. Pentothal sodium in a 5 per cent aqueous solution was administered intravenously. Anesthesia was carried to the third stage according to the criteria of Lundy.²² Twenty-three to twenty-eight milligrams of pentothal sodium per kilogram of body weight were required.

In five dogs there was a transient reduction in tonus and a decrease in motility immediately after injection of the drug. In all of these observations tonus and motility had returned to normal before the animal was awake. In two dogs gastric tonus and motility were unaffected by third stage anesthesia produced by the intravenous injection of pentothal sodium.

11. *Intravenous Administration of Pentothal Sodium Supplemented With Nitrous Oxide-Oxygen*.—The effect on gastric motor activity of intravenous administration of pentothal sodium supplemented with nitrous oxide-oxygen was studied in seven dogs. Pentothal sodium in doses of 15 to 20 mg. per kilogram of body weight was given intravenously and the animals were allowed to breathe a gas mixture composed of equal parts of nitrous oxide and oxygen. In all observations there was no effect on gastric tonus or motility.

12. *Spinal Anesthesia* (Fig. 3b).—Observations were made on seven dogs. To facilitate lumbal puncture the dogs were placed on the Delahanty table as modified by Gross and Lundy. A 2.5 per cent solution of procaine hydrochloride in doses of 3.3 to 6.8 mg. per kilogram of body weight was used. Injection of anesthetic solution was done between the spines of the last thoracic and first lumbar, or between those of the first

be as complete as that observed with ether. The effect on gastric motor activity was strikingly similar to that of ether. Gastric tonus was greatly diminished and motility entirely abolished. The average time required for motor activity to return to normal in all observations was two hours and forty-five minutes.

7. *Cyclopropane-Oxygen Supplemental to a Basal Anesthetic of Avertin With Amylene Hydrate.*—Observations were made on four dogs. The effect of cyclopropane-oxygen on gastric tonus and motility was not altered when these agents were supplemental to a basal anesthetic of

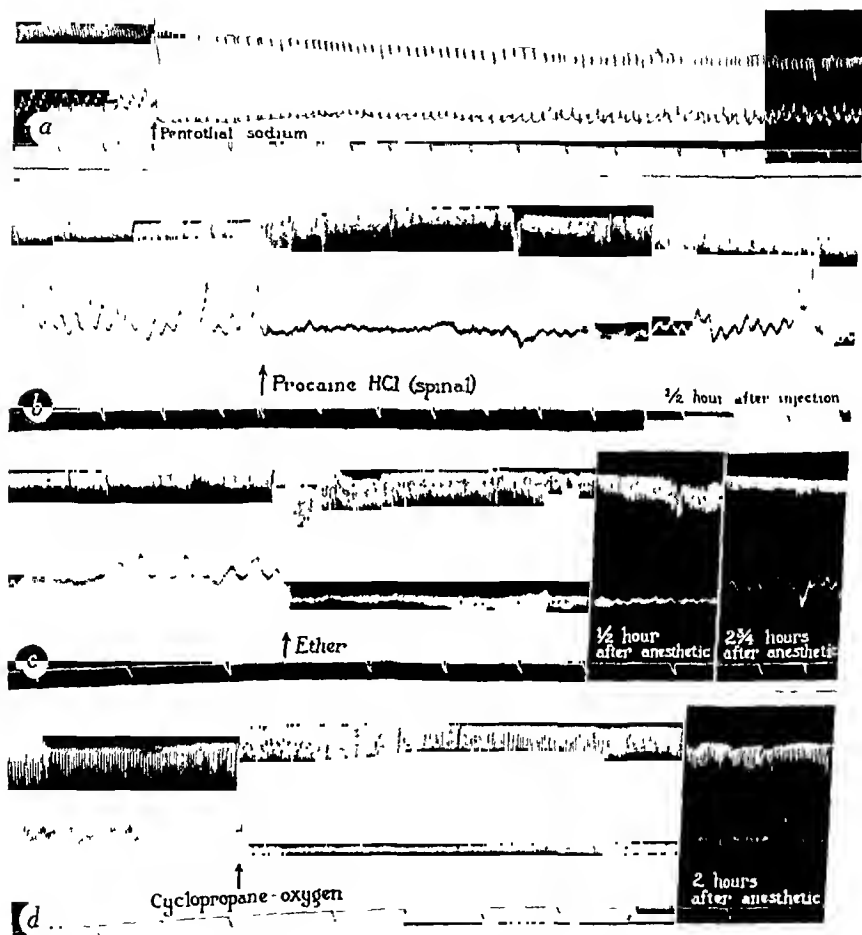


Fig. 3.—Effect of anesthesia on gastric contractions. *a*, Pentothal sodium anesthesia, Dog 5 (weight 12.5 kg.). Pentothal sodium 0.3 Gm. in 5 per cent aqueous solution given intravenously.

b, Spinal anesthesia, Dog 7 (weight 15.5 kg.). Procaine hydrochloride, 75 mg. in 3 c.c. physiologic salt solution injected in subarachnoid space between spines of last thoracic and first lumbar vertebrae; sensory loss demonstrated at upper thoracic level.

c, Ether anesthesia after bilateral splanchnicectomy and double vagotomy, Dog 6 (weight 12 kg.); third stage anesthesia indicated by arrow.

d, Cyclopropane-oxygen anesthesia after bilateral splanchnicectomy and double vagotomy, Dog 8 (weight 11 kg.); third stage anesthesia indicated by arrow.

by bleeding under pentothal sodium anesthesia and at necropsy an attempt was made to determine whether the splanchnic or vagus nerves had regenerated. It was found that the vagi had not regenerated. This is in accord with the work of Vanzant who, using the same technique for double vagotomy that was employed in this study, showed that there was no regeneration of the vagus nerves of the dog when examined two to three years after vagotomy. In one dog on which necropsy was performed eleven weeks after splanchnicectomy, no tissue replacement could be found between the severed ends of the nerves. In the remaining five dogs on which splanchnicectomy had been done, some fairly well-defined strands of replacement tissue were found at the site of the original denervation. Necropsy was performed on these five dogs longer than five months after splanchnicectomy. In two dogs this tissue replacement was carefully resected and prepared for microscopic study. Nerve tissue was found in the entire course of the site of the original operation. Necropsy was performed on these two dogs eight months after splanchnicectomy. This observation undoubtedly represented regeneration of these nerves. Most of the experiments carried out after splanchnicectomy were done within a period of eight weeks after denervation and many were done as soon as four and one-half weeks after denervation. It is believed that very little, if any, regeneration of these nerves had taken place by that time, especially in view of the fact that very extensive splanchnicectomy was performed.

There was very little evidence to indicate that the decrease in gastric tonus and motility was dependent on the relative quantity of oxygen in the blood and tissues during anesthesia. It is true that with nitrous oxide-oxygen, in order to anesthetize the dog deeply enough to permit satisfactory observation, it was necessary to increase the concentration of nitrous oxide to the point of cyanosis. Just what effects were due to anoxia and what effects were due to the concentration of nitrous oxide in the blood is impossible to say. Cyclopropane-oxygen anesthesia depressed gastric motor activity much more than did ethylene-oxygen anesthesia, even when some cyanosis was produced with the latter agent.

Apparently the depth is more important than the duration of anesthesia in relation to the effects on gastric tonus and motility. Increasing the duration of ether anesthesia fivefold prolonged the depressing effect very little. This is in agreement with the work of Cannon and Murphy⁸ on cats. These workers measured the gastric emptying time by means of the roentgenoscopic method after etherization. They found that anesthesia maintained for one-half hour prolonged gastric emptying very nearly as long as when anesthesia was maintained triple that time.

A rather striking individual susceptibility to the depressing effect on gastric tonus and motility was exhibited by the dogs in this investigation. In some dogs there was a tendency for a quicker return of motor activity no matter what anesthetic was employed; in others a relatively greater

and second lumbar vertebrae. The criteria used to determine a successful experiment were the free aspiration of spinal fluid before and after the injection, complete paralysis of the hind legs, and the demonstration of a sensory loss at the upper thoracic level.

In four dogs there was a diminution of the amplitude of gastric contractions with no reduction in tonus. In three dogs, in addition to a diminution in the amplitude of contractions there was a moderate reduction in tonus. Gastric tonus and motility returned to normal about the time the first movements of the hind legs were noted.

B. Effects of Anesthetics on Gastric Tonus and Motility After Splanchnicectomy and Vagotomy.

The effect of the anesthetics used in the innervated group of animals was studied in four dogs on which bilateral splanchnicectomy and double vagotomy had been performed, in two dogs on which bilateral splanchnicectomy only had been performed, and in two dogs on which double vagotomy only had been performed. In all three of these groups of denervated animals the effect of anesthetics on gastric tonus and motility was essentially the same as observed in the innervated group of animals (representative tracings, Fig. 3c and d).

COMMENT

It can be seen that anesthetics had either a depressing effect on gastric tonus and motility or no effect at all. The decrease in activity was, in a general way, directly proportional to the degree of anesthesia produced, regardless of the agent used. Anesthesia carried to plane 2 of the third stage by any of the inhalation anesthetics, whether employed alone, in combination with another inhalation anesthetic, or supplemental to a basal anesthetic of avertin with amylene hydrate, caused a marked reduction in gastric tonus and complete cessation of motility. Since the effect of these anesthetics in the three groups of denervated animals was essentially the same as in the innervated group, it was concluded that the effect was primarily on the peripheral gastric motor mechanism and was not mediated through the splanchnic or vagus nerves.

It is believed that the reduction in gastric tonus was not an expression of decreased intra-abdominal pressure caused by loss of tone of the abdominal musculature. In many experiments, gastric tonus did not return to normal for as long as several hours after the animal had completely regained use of the skeletal muscles.

The question may be asked whether the experiments done after denervation were carried out before the vagus and splanchnic nerves had regenerated. The recent observations of Hinsey and associates and those of Hollinshead and Finkelstein have served to emphasize the importance of functional control of regeneration in work on sympathectomized animals. When all the experiments in the present investigation were finished, the dogs on which denervation had been performed were killed

Premedication with morphine and atropine definitely prolonged the depressing effect of ether. From a review of some of the experimental work relative to the action of morphine and atropine on gastric motor activity, no general conclusion concerning the action of morphine on gastric tonus and motility can be made, although it is generally conceded that atropine causes a decrease in activity.^{5, 18, 24, 32, 33, 35, 36, 38} This is in part understandable when consideration is given to the method of investigation and the species of animal investigated. When the action of morphine was studied in the dog by means of the balloon-recording method,^{5, 32} the results were fairly consistent. There was a marked decrease in activity lasting for several hours. In the light of these observations it would appear that the prolongation of the depressing effect of ether on gastric tonus and motility after premedication with morphine and atropine which was observed in the present study could be explained.

When the action of morphine on man was studied, most of the available evidence showed that the action of morphine on the walls of the stomach was predominantly motor.^{5, 35, 36, 38} There is undoubtedly a species difference. Veach, on the basis of his results in human subjects, recommended the use of morphine in the treatment of acute dilatation of the stomach. In view of the work of Schapiro and that of Van den Velden, which showed that gastric emptying in man may be considerably prolonged by morphine, presumably by tonic contraction of the pylorus, the rationale of the use of morphine in the treatment of acute gastric dilatation is open to question.

If the same situation obtains in man as was found in the dog, it may be seen that considerable gastric atony may follow deep general anesthesia, presumably by a direct effect on the peripheral gastric motor mechanism. This should take on more significance if it is true that the human gastric motor mechanism is depressed more by anesthesia than that of the dog³¹ and if the same individual susceptibility to anesthesia prevails in man as was observed in the dog. It may be that, if block anesthesia of peripheral nerves were employed in conjunction with a lesser degree of general anesthesia, there would be less postoperative gastric atony attributable to the anesthetic agents.

Dragstedt's¹² contention that the loss of gastric tonus in acute postoperative gastric dilatation is a result of the effect of operative trauma plus the effect of anesthesia may be true. It is reasonable to suppose that each of these factors would take on relatively greater or less significance in a given case, depending on the degree of anesthesia and the nature and extent of the operative trauma. In this connection the work of Cannon and Murphy⁸ is of interest. These investigators, in studying the conditions attending operation as possible causes of postoperative paralysis of the alimentary canal, measured the degree of discharge of food from the stomach of the cat by the roentgenoscopic method. They found that etherization caused some delay in emptying. Etherization plus laparotomy, exposure of the gut to the air, and minimal cooling

time elapsed before tonus and motility returned to normal after discontinuance of the anesthetic. This difference of reaction to anesthesia did not seem to be dependent on the nutritional state, emotional make-up, age or weight of the animal, nor on the type of gastric contractions observed during the preanesthetic control period.

We have no explanation for the decrease in gastric motor activity which was observed during spinal anesthesia. Before this work was undertaken, it was thought that this method would cause an increase in activity similar to its reported effect on the small intestine. The explanation given for the increase in activity in the small bowel during spinal anesthesia is that the inhibitory influence mediated through the splanchnic nerves is abolished by blocking conduction through these nerves with procaine.^{3, 26, 29} After observing a decrease in gastric activity during the course of the first few experiments, we felt that the spinal anesthesia was not sufficiently high to involve the splanchnic supply to the stomach. This idea was given weight by the work of Barron, Curtis, and Lauer. These workers observed a decrease in gastric tonus and motility with the balloon-recording method in patients during herniorrhaphy under spinal anesthesia. They did not observe any evidence of splanchnic paralysis and concluded that the gastric paresis was due to reflex stimulation of the splanchnic nerves during the course of the operation.

Accordingly, experiments were continued in which progressively greater amounts of procaine were employed until a definite sensory loss was demonstrated in the region of the upper thoracic level and in a few instances at the lower cervical level. This proved to make no difference in the effects on gastric tonus and motility; activity was depressed in all experiments. The excitement which may attend the performance of spinal anesthesia in some instances was ruled out as a possible cause for these results early in the course of the experiments when the technique of spinal anesthesia on the dog was being learned. Many unsuccessful attempts to insert the needle into the subarachnoid space did not affect gastric activity.

The fact that the same decrease in gastric activity during spinal anesthesia was observed after splanchnicectomy led to a consideration of some other mechanism not dependent on the presence of the splanchnic nerves to account for this effect. The possibility that procaine circulating through the blood stream might affect the peripheral gastric motor mechanism directly was considered but the injection of large amounts of procaine in the region of the spinal cord, but not in the subarachnoid space, failed to decrease gastric tonus and motility. What effect a lowering of the blood pressure due to spinal anesthesia would have is not known. There is the possibility that the decrease in gastric activity might be dependent on the effect of spinal anesthesia on the small bowel. It has been shown, for instance, that handling of the small bowel causes a decrease of gastric motor activity whether the splanchnic nerves are intact or not.⁹

The effect of these anesthetics on gastric tonus and motility was essentially the same after splanchnicectomy or vagotomy or both, as was observed in the innervated animal. It was concluded that this effect was not mediated through the vagus or splanchnic nerves and was therefore primarily on the peripheral gastric motor mechanism.

There was very little evidence to indicate that the decrease in gastric tonus and motility was dependent on the relative quantity of oxygen in the blood and tissues during anesthesia.

A rather striking individual susceptibility to the depressing effect on gastric motor activity was exhibited by the dogs in this investigation. In some dogs there was a tendency for a quicker return of activity no matter what anesthetic was employed; in others a relatively greater time elapsed before tonus and motility returned to normal.

Premedication with morphine and atropine definitely prolonged the depressing effect of ether.

Apparently the depth is more important than the duration of anesthesia in relation to the effects on gastric tonus and motility. Increasing the duration of ether anesthesia fivefold prolonged the depressing effect very little.

No explanation is given for the decrease in gastric motor activity which was observed during spinal anesthesia.

The possible role of anesthesia in acute gastric dilatation as observed clinically is discussed.

REFERENCES

1. Allison, R. G.: Dilatation and Atony of the Stomach in Severe Diabetes, *Radiology* 3: 222-224, 1924.
2. Báron, Alexander, and Bársony, Theodor: Über die Einwirkung der Chloroform- und Äthernarkose auf die motorischen Magenfunktionen, *Arch. f. d. ges. Physiol.* 158: 464-477, 1914.
3. Barron, L. E., Curtis, G. M., and Lauer, Bernard: Influence of Laparotomy on the Gastric Motor Mechanism of Man, *Arch. Surg.* 35: 675-693, 1937.
4. Best, C. H., and Taylor, N. B.: *The Physiological Basis of Medical Practice*, Ed. 2, Baltimore, 1939, Williams & Wilkins Company, p. 794.
5. Bisgard, J. D., and Johnson, E. K.: The Influence of Certain Drugs and Anesthetics Upon Gastro-intestinal Tone and Motility, *Ann. Surg.* 110: 802-822, 1939.
6. Boyd, William: *A Text-book of Pathology: An Introduction to Medicine*, Ed. 3, Philadelphia, 1938, Lea & Febiger, p. 538.
7. Brown, Alfred: Discussion, *Ann. Surg.* 110: 820-821, 1939.
8. Cannon, W. B., and Murphy, F. T.: The Movements of the Stomach and Intestines in Some Surgical Conditions, *Ann. Surg.* 43: 512-536, 1906.
9. Cannon, W. B., and Murphy, F. T.: Physiologic Observations on Experimentally Produced Ileus, *J. A. M. A.* 49: 840-843, 1907.
10. Carlson, A. J.: *The Control of Hunger in Health and Disease*, Chicago, 1916, University of Chicago Press, 319 pp.
11. Cutting, R. A.: Dilatation of the Stomach, *Am. J. Surg.* 12: 597-610, 1931.
12. Dragstedt, L. R.: Acute Dilatation of the Stomach. In Lewis, Dean, *Practice of Surgery*, Hagerstown, Maryland, 1940, W. F. Prior Company, Inc., vol. 6, chap. 10, pp. 1-18.
13. Dragstedt, L. R., Montgomery, M. L., Ellis, J. C., and Matthews, W. B.: The Pathogenesis of Acute Dilatation of the Stomach, *Surg., Gynec. & Obst.* 52: 1075-1086, 1931.
14. Essex, H. E., and Lundy, J. S.: A Technique That Facilitates Lumbar Puncture in the Dog, *Proc. Soc. Exper. Biol. & Med.* 29: 751-753, 1932.
15. Eusterman, G. B., and Balfour, D. C.: *The Stomach and Duodenum*, Philadelphia, 1935, W. B. Saunders Company, p. 703.

caused no more delay in gastric emptying than did ether alone. By far the most striking effects were seen after handling of the digestive organs. Even with the most gentle handling within the peritoneal cavity or under warm salt solution no gastric peristalsis was seen and no food left the stomach for hours.

If comparatively little gastric atony were found to develop postoperatively among patients who had had pentothal sodium, nitrous oxide-oxygen alone, or ethylene-oxygen alone, it might be argued, on the basis of the results of this investigation, that this was because these agents do not depress gastric motor activity to any great extent. While this might be true in part, it does not tell the whole story. By virtue of the scope of operation permitted under these agents, the operative trauma is different from the trauma in those procedures requiring complete muscular relaxation. Certainly the extent of trauma would be less in most cases. More experimental work is definitely needed to clarify the effects that various operative procedures per se have on gastric motor activity.

There is probably some gastric atony after every operative procedure but the occurrence of the more advanced stages of acute dilatation of the stomach appears to be infrequent at the present time. Aside from any change in the etiologic factors in acute gastric dilatation, the lessened incidence of the condition would seem to be due in a large measure to better postoperative care. The aspiration of the collected fluid and gas from the stomach and more general application of the principle of continuous gastric aspiration as advocated by Paine and Wangenstein, together with the replacement of lost fluid and electrolytes, probably have had much to do with the lessened incidence of this grave postoperative complication.

SUMMARY AND CONCLUSIONS

In order to evaluate more properly the factor of anesthesia in acute gastric dilatation a comparative study was made of the effects of anesthetics on gastric tonus and motility in the trained dog. Studies were made on animals in which the extrinsic gastric nerves were present and after vagotomy and splanchnicectomy. The apparatus used to record the motor activity of the stomach was the balloon-bromoform manometer apparatus. The balloon was inserted into the stomach through a Mann-Bollman type of fistula.

It was found that anesthetics had either a depressing effect on gastric tonus and motility or no effect at all. The decrease in activity was in a general way directly proportional to the degree of anesthesia produced, regardless of the agent used. Anesthesia carried to plane 2 of the third stage by any of the inhalation anesthetics, whether employed alone, in combination with another inhalation anesthetic, or supplemental to a basal anesthetic of avertin with amylene hydrate, caused a marked reduction in gastric tonus and complete cessation of motility.

TRAUMATIC RUPTURE OF THE PREGNANT UTERUS RESULTING FROM AN AUTOMOBILE ACCIDENT

R. B. WOODHULL, M.D., MINOT, N. D.

(From the Northwest Clinic)

IN THIS modern machine age, when more than thirty thousand persons annually meet their death in highway accidents in the United States alone, it is surprising to discover that traumatic rupture of the pregnant uterus from this cause has received practically no attention. Doubtless, many cases have not been reported in literature, but because of the rarity of this obstetrical calamity, and its numerous problems in diagnosis and treatment, the following case was thought to be of interest.

The scope of this paper is limited to those cases of traumatic rupture of the pregnant uterus from external violence alone. No consideration has been paid to spontaneous rupture, rupture through cesarean section or myomectomy scars, or to those uteri which were ruptured as the result of operative attempts at delivery or abortion, or as the result of obstructed labors.

A very complete review of the literature was made by Jarosehka in 1929,¹ and a series of forty cases of traumatic uterine rupture previously reported by Estor and Pueck were studied. To this series he added one case of his own from the Prague Clinic.

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Another case was added by Lazard and Kliman⁴ in 1936, of a primipara, eight months pregnant, who fell down steps striking her abdomen on the edge of the steps. Severe abdominal pain was noted for one hour, later the pain being referred to the shoulder. This was followed by moderate vaginal bleeding and cessation of fetal movements. On admission to the hospital the abdomen was markedly distended, but fetal parts were clearly palpable beneath the skin. When the abdomen was opened the peritoneal cavity was found full of blood, with the fetus

16. Guedel, A. E.: *Inhalation Anesthesia: A Fundamental Guide*, New York, 1937, The Macmillan Company, p. 14.
17. Hinsey, J. C., Phillips, R. A., and Hare, Kendrick: *Observations on Cats Following Pre- and Postganglionic Sympathectomies*, *Am. J. Physiol.* 126: 534, 1939.
18. Hirsch, Alfred: *Zur Kenntnis der Wirkung des Morphins auf den Magen*, *Zentralbl. f. inn. Med.* 22: 33-47, 1901.
19. Hollinshead, W. H., and Finkelstein, H.: *Regeneration of Nerves to the Adrenal Gland*, *J. Comp. Neurol.* 67: 215-220, 1937.
20. Kaufman, J., and Levine, I.: *Acute Gastric Dilatation of Stomach During Attack of Migraine*, *Radiology* 27: 301-302, 1936.
21. Kelling, Georg: *Ueber den Mechanismus der acuten Magendilatation*, *Arch. f. klin. Chir.* 64: 393-417, 1901.
22. Lundy, J. S.: In Beecher, K. B., *The Physiology of Anesthesia*, London, 1938, Oxford University Press, p. 12.
23. Lundy, J. S., Tuohy, E. B., Adams, R. C., Monsel, L. H., and Seldon, T. H.: *Annual Report for 1939 of the Section on Anesthesia: Including Data on Blood Transfusion and a Review of Anesthetic Agents and Methods From 1924 to 1939, Inclusive*, *Proc. Staff Meet., Mayo Clin.* 15: 241-254, 1940.
24. Magnus, R.: *Die stopfende Wirkung des Morphins*, *Arch. f. d. ges. Physiol.* 122: 210-250, 1908.
25. Mann, F. C., and Bollman, J. L.: *A Method for Making a Satisfactory Fistula at Any Level of the Gastro-intestinal Tract*, *Ann. Surg.* 93: 794-797, 1931.
26. Markowitz, J., and Campbell, W. R.: *The Relief of Experimental Ileus by Spinal Anesthesia*, *Am. J. Physiol.* 81: 101-106, 1927.
27. Miller, G. H.: *The Effects of General Anesthesia on the Muscular Activity of the Gastro-intestinal Tract: A Study of Ether, Chloroform, Ethylene and Nitrous Oxid*, *Anesth. & Analg.* 5: 225-234, 1926.
28. Mousel, L. H., and Seldon, T. H.: *A Gas Machine for the Anesthetization of Small Laboratory Animals*, *Proc. Soc. Exper. Biol. & Med.* 42: 248-249, 1939.
29. Ochsner, Alton, Gage, I. M., and Cutting, R. A.: *Treatment of Ileus by Splanchnic Anesthesia; Preliminary Report of Experimental Study*, *J. A. M. A.* 90: 1847-1853, 1928.
30. Paine, J. R., and Wangensteen, O. H.: *The Necessity for Continuous Suction to Inlying Nasal Tube for Effectual Decompression or Drainage of Upper Gastro-intestinal Tract*, *Surg., Gynec. & Obst.* 57: 601-611, 1933.
31. Payer: Quoted by Miller, G. H.²⁷
32. Plant, O. H., and Miller, G. H.: *The Effect of Morphine and Somo of the Other Opium Alkaloids on the Muscular Activity of the Alimentary Canal. III. Action of the Stomach in Unanesthetized Dogs*, *J. Pharmacol. & Exper. Therap.* 32: 413-435, 1928.
33. Schapiro, Nicolai: *Über die Wirkung von Morphinum, Opium und Pantopon auf die Bewegungen des Magen-Darm-Tractus des Menschen und des Tieres*, *Arch. f. d. ges. Physiol.* 151: 65-96, 1913.
34. Stobie, William: *Acute Gastric Dilatation Associated With Pulmonary Tuberculosis*, *Brit. M. J.* 1: 67-68, 1929.
35. Tezner, Otto, and Turol, Max: *Pharmakologische und physiologische Studien am überlebenden menschlichen Magen*, *Ztschr. f. d. ges. exper. Med.* 12: 275-287, 1921.
36. Van den Velden, R.: *Zur Pharmakologie der Magenmotilität*, *München. med. Wehnschr.* 56: 1667, 1909.
37. Vanzant, Frances R.: *Late Effects of Section of the Vagus Nerves on Gastric Acidity*, *Am. J. Physiol.* 99: 375-378, 1932.
38. Veach, H. O.: *The Antagonistic Action of Morphine and Atropine on the Human Stomach*, *J. Pharmacol. & Exper. Therap.* 61: 230-239, 1937.
39. Walton, A. J.: *Acute Dilatation of the Stomach*. In *Nelson New Loose-leaf Surgery*, New York, 1941, Thos. Nelson & Sons, vol. 5, chap. 2, pp. 80-81.

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lying in the intact amniotic sac. The placenta had been completely separated from the uterus through a large rent in the posterior uterine wall. The uterus was firmly contracted. A supravaginal hysterectomy was done and the patient recovered.

Snidow⁵ reported a similar case of multipara who had fallen down a flight of stairs. The patient stated that there was no pain immediately after the fall, but that one hour later she began having severe abdominal cramps and a slight amount of vaginal bleeding. Eight hours later there was a profuse vaginal hemorrhage followed by profound shock. At operation the abdomen was filled with blood with the fetus lying free in the abdominal cavity. There was a longitudinal tear in the midline posteriorly extending from the fundus of the uterus to the internal os. The placenta was adherent to the anterior uterine wall. This patient also made an uneventful recovery after supravaginal hysterectomy. It was found in reviewing this patient's past history that she had had a toxemia with her previous pregnancy, and a subsequent endometritis for several weeks after delivery.

One further case of ruptured uterus by indirect injury is given by Stapleton⁶ from New Delhi, India, of a Hindu primipara, aged 17 years, at full term, who had fallen ten feet from a first floor veranda. The patient fell on her right side, being only stunned for several minutes. She stayed in bed for the next few days, had several episodes of nausea and vomiting, and complained of pain over the right hip and loin. Five days later she was again up and about and able to take food. According to the patient, fetal movements were felt three to four days after the accident. There was a slight bloody vaginal discharge for four days prior to admission. At this time the relatives said they did not think the baby was still alive because the abdomen was getting smaller. Examination showed a term pregnancy with the head in the left occipito-anterior position, at the pelvic brim. There were no fetal movements or heart tones. No abdominal distention or tenderness was elicited. Vaginal examination presented a long, closed cervix. Medical induction was attempted with castor oil, quinine, and enemas. After two days there were still no labor pains and only a moderate bloody "show"; the temperature was normal. The following day a piece of membrane was seen in the vagina, and the head bones of a macerated fetus could be felt above the internal os. At laparotomy a macerated fetus lying free among the intestines was removed. The placenta was located low down in front of a small, firmly contracted uterus, the edges still attached to a large, gaping, transverse tear across the fundus. The uterus had retracted and involuted in the shape of a cup. The peritoneal cavity contained a small amount of brown free fluid, but no signs of recent bleeding or general peritonitis. The rent in the uterine wall was hastily repaired and the wound closed with drains. The patient later developed pleurisy and pneumonia with a separation of the abdominal wound and fecal fistula. This subsequently closed and the girl recovered.

CASE REPORT

Mrs. J. J. (54,634) is a primipara, aged 20 years. She had the usual childhood diseases without complications, and an appendectomy through a McBurney incision in 1939. Her menstrual periods had been quite irregular since their onset at the age of 13 years, recurring every three or four weeks, but with normal flow of four to five days. She had had no serious illnesses, pelvic infections, or curettages. The patient's last menstrual period was on Feb. 6, 1940, making her estimated date of confinement Nov. 13, 1940. Fetal heart tones were heard at her regular ante-partum visit in July and August, and the uterus had enlarged normally, corresponding to the term of pregnancy. On September 7, she was riding in the front seat of a car driven by her sister-in-law, when they were involved in a head-on collision. The patient was thrown out of the right door, landing on her back at the side of the road. The car fell across the dorsal surface of her thighs, which were flexed upon the abdomen. The patient was not unconscious and was able to pull herself back into the car after it was lifted free. She was then carried to a passing car and brought immediately to the hospital. On admission she complained of severe upper abdominal pain "just as if everything was going to drop out." The temperature was 99.4° F.; pulse, 130; and respirations, 28. The blood pressure was 90/70, with 67 per cent hemoglobin, and 3,780,000 red blood cells. The abdomen was tender but not rigid, with no distention. The uterus was enlarged to the size of a seven months' pregnancy and fetal parts were not easily felt. There was no vaginal bleeding and no fetal heart tones were heard, but the patient stated that she felt fetal movements after her admission to the hospital. These were never detected by either the intern or the examining physician. A small laceration on the dorsal surface of the right thigh was dressed but no sutures were necessary. The patient was placed in Trendelenburg position and an ice bag applied to the abdomen. Intravenous fluid and a blood transfusion were given as quickly as possible. In two hours the blood pressure had risen to 112/84 and the pulse was 92. She still complained of abdominal pain but her general condition seemed improved. The possibility of uterine rupture was considered at this time, but in view of her rapid recovery on only supportive treatment, premature separation of the placenta with fetal death was thought to be a more likely diagnosis. There was still no external vaginal bleeding. Morphine was given for the abdominal pain. X-ray of the abdomen showed fractures involving the transverse processes of the five lumbar vertebrae on the right side, and fractures of the transverse processes of the fourth and fifth lumbar vertebrae on the left. A scout plate of the abdomen about ten days following the accident showed one fetal skeleton of about six months gestation with overlapping of the skull bones. The temperature during the first two weeks of hospitalization ranged between 99.6° and 101° F. and the pulse from 78 to 122. The patient continued to complain of some upper abdominal pain which was momentarily relieved with narcotics. The appetite remained good and the bowel function regular. Three weeks following the accident, when I saw the patient for the first time, pelvic examination revealed a long, firm, undilated cervix. There was no vaginal discharge or bleeding. On bimanual examination the uterus was felt to be about the size of a four months pregnancy and separated from a larger mass posterior and to the right. On Oct. 8, 1940, one month following the accident, a laparotomy was performed through a lower midline incision. The uterus and all pelvic organs were walled off by a fibrinous exudate. There were loops of bowel adherent to underlying pelvic structures. After these were separated the fetus was found lying free in the pelvic cavity, and there was a complete laceration of the uterus, extending down the posterior surface from the fundus to the cervix. The edges were ragged and widely separated, leaving a defect in the wall about 8 cm. in diameter. The placenta had been partially delivered through the laceration, but the cord was still firmly attached to the fetus. This tissue was extremely friable and broke into

many pieces when an attempt was made to remove it from the pelvic structures. Several pieces which were densely adherent to loops of bowel and the pelvic wall were left in situ. The fetus appeared well developed, about 40 cm. in length, but had undergone considerable maceration. There was no free fluid in the abdomen. It was found impossible to repair the rent in the uterine wall, consequently a supra-vaginal hysterectomy was done. The abdomen was closed in layers without drains. The postoperative course was complicated by a severe bronchopneumonia which was successfully treated with sulfapyridine. The patient was discharged from the hospital on the seventeenth postoperative day, only to be readmitted Nov. 26, 1940, with a partial intestinal obstruction. This was relieved with a Miller-Abbott tube. When last seen for her checkup examination June 2, 1941, she stated that she had been feeling well. Her appetite was good and bowel habits regular. The abdominal wound was well healed. There had been no vaginal bleeding or discharge. Pelvic examination showed the cervix to be clean and well suspended. The right ovary was palpable deep in the right fornix. The left fornix was clear. Rectal examination was negative.

Histologic study of the uterine muscle showed nothing abnormal except that the myometrium contained many highly dilated blood spaces. The muscle fibers were increased in diameter and somewhat tortuous from shortening. The endometrium was hypertrophied and densely infiltrated with small round cells. Buried in the endometrium were masses of necrotic placental villi.

DISCUSSION

It seems safe to assume that uterine rupture in this case occurred at the time of the accident due to the blow upon the abdomen. After the fetus and a portion of the placenta were extruded into the abdominal cavity, the uterus apparently clamped down very rapidly, allowing for only a minimal loss of blood. Fetal death must necessarily have taken place within several minutes following the accident. From the standpoint of diagnosis, this patient did not exhibit the usual signs associated with rupture of the uterus, namely, evidence of intra-abdominal hemorrhage, shock, accumulation of blood under the diaphragm, abdominal rigidity, pain radiating to the shoulder, or vaginal bleeding. The absence of these signs masked the true gravity of her condition, and led to the early mistaken diagnosis. It was only after the inflammatory reactions and toxic absorption were in evidence that operation seemed advisable.

Once the diagnosis of uterine rupture is made, the controversial question of whether to remove the uterus or to attempt a repair must be considered. The parity of the patient and desire for future pregnancies must necessarily influence our decision. If she is a primipara and is unwilling to gamble with the possibility of uterine rupture with subsequent pregnancies, preservation of the organ by suturing the laceration as effectively as possible may be in order. Many times this procedure is more time-consuming and hazardous than a rapid hysterectomy, especially when the patient is such a poor operative risk. Certainly, hysterectomy lessens the chances of infection and speeds the postoperative recovery. When the edges of the rent are widely separated and the

myometrium so extremely friable, as in the case reported, satisfactory uterine repair is impossible and hysterectomy must be done.

As has been mentioned by Orthner, traumatic lacerations of the uterus are due to a sudden increase in intra-abdominal pressure, which is transmitted to the uterus. The pregnant uterus, lying as it does, unprotected by the bony pelvic framework, is most prone to rupture in the fundal portion. This is the weakest point in the last trimester of pregnancy because of the vascularity of the uterine wall directly beneath the placenta.

Uterine rupture is designated as complete or incomplete depending upon whether or not the viscerai peritoneum is opened. A complete laceration extends through the entire thickness of the endometrium, myometrium, and peritoneum, making a direct communication through the vagina to the peritoneal cavity. This is far more serious than the incomplete type in which the peritoneum remains intact. However, the maternal death rate in all types of uterine rupture ranges between 60 and 80 per cent, and reaches nearly 100 per cent for those cases not operated upon.

The classical sign of rupture of the pregnant uterus following severe abdominal trauma is evidence of bleeding, either external vaginal or intra-abdominal. This is accompanied by severe abdominal pain with tenderness and rigidity, usually of the rebound type. This denotes signs of peritoneal irritation from intra-abdominal hemorrhage. Very often a fluid level of blood in the peritoneal cavity may be outlined. If fetal parts are readily palpable directly beneath the skin, the diagnosis of uterine rupture should be suspected. These signs will be found accompanying those pointing to fetal death. In those cases exhibiting profuse external bleeding without signs of peritoneal reaction, accidental hemorrhage or placenta praevia must be thought of in spite of a history of abdominal trauma. In earlier pregnancy where signs of intraperitoneal hemorrhage are present, ruptured ectopic pregnancy or rupture of a poorly developed uterine horn may be the cause.

When uterine rupture occurs in the lower uterine segment, bimanual palpation for the round ligaments may give some clue to the diagnosis. On the side of rupture the ligament will be absent, while the opposite ligament may be readily palpable.

In spite of the satisfactory outcome of the case reported, the importance of early diagnosis and prompt operative treatment cannot be overemphasized, if the maternal mortality is to be reduced. The first and foremost effort should be exerted toward the control of shock by intravenous fluids and blood transfusions. This is frequently a life-saving measure until the patient's condition will warrant a laparotomy. Heroic efforts to control blood loss by clamping of the uterine arteries per vagina has been attempted by some men with success, while preparations for adequate surgery are in progress.

SUMMARY

1. Attention is directed to the rarity of traumatic rupture of the pregnant uterus from automobile accidents.

2. The salient points in the prompt diagnosis and treatment of this condition are briefly discussed.

REFERENCES

1. Jaroschka, K.: Med. Klin. 25: 709, 1929.
2. DeLee, J. B.: Am. J. Obst. & Gynec. 1904.
3. Orthner, F.: München. med. Wchnschr. 80: 1248, 1933.
4. Lazard, E. M., and Kliman, F. E.: California & West. Med. 45: 482, 1936.
5. Snidow, F. A.: Am. J. Obst. & Gynec. 35: 751, 1935.
6. Stapleton, Grace: Brit. M. J. 2: 367, 1937.
7. Atakam, A. M.: Anadolu klin. 6: 143.

EPISPADIAS WITH INCONTINENCE IN THE MALE

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EPISPADIAS is fortunately, one of the rarest of congenital anomalies. Because of its rarity it is mentioned only casually in most urologic textbooks and in the past fifty years few articles dealing with this anomaly have appeared in the medical literature. However rare this condition may be from a statistical standpoint, to the individual so afflicted it is a tragedy, particularly if associated with urinary incontinence. The wet clothing and uriniferous odor resulting from this condition inevitably bring about social ostracism. This, together with the penile deformity, usually causes deep-seated psychic trauma. Most urologists see only a few such cases in a lifetime of practice. We must, therefore, rely in great part on both the successful and unsuccessful experiences of others in treating this malady.

Congenital epispadias is characterized by the abnormal location of the urethral opening on the dorsum of the penis. It may be situated anywhere from the glans penis to the penopubic junction and, depending on its location, epispadias may be classified as balanic, penile and complete, or penopubic. In contrast to hypospadias, the balanic type of epispadias is rarest, penile epispadias being slightly more common, and penopubic the commonest of the three. According to Hinman,¹ hypospadias occurs about 150 times as often as epispadias. As hypospadias is seen about once in every 300 or 350 males the incidence of epispadias is about one in 45,000 to 50,000 males. Nove-Josserand,² in fifteen years of urological practice, saw four cases of epispadias and sixty cases of hypospadias. Since the opening of the Duke University Hospital, approximately 168,000 patients, both male and female, have been seen. Among the male patients in this group there have been seventy-one cases of hypospadias and five cases of epispadias. All five cases were of the penopubic type, three having complete urinary incontinence and two having urinary control.

Complete epispadias is often associated with absolute incontinence of urine, which is due to a congenital lack of fusion of the internal and external urethral sphincters anteriorly. The sphincters and prostatic urethra may be so patulous as to easily admit the index finger. The symphysis pubis is characteristically separated, there being a heavy fibrous band of tissue joining the separated halves. The penis is of normal size or larger than normal and is drawn acutely upward to lie

against the abdominal wall. The prepuce is redundant on the ventrum of the penis and lacking on its dorsum. The corpus spongiosum is absent and the corpora cavernosa are not firmly attached to each other but may be easily separated. The glans penis exhibits a defect or groove along its dorsal surface which is continuous along the dorsum of the penis with a depression between the corpora cavernosa which is lined with mucous membrane, an embryologic remnant of the urethral floor. This trough is continuous proximally with an infundibulum or funnel-shaped opening which extends inward beneath the symphysis pubis to become continuous with the prostatic urethra. The testicles are usually well descended and normal. The ejaculatory ducts are patent and ejaculation may occur into the bladder. The power of erection is usually present but coitus and procreation are virtually impossible. The bladder itself is normally formed and innervated but usually smaller than normal because of disuse. The internal vesical sphincter is widely dilated so that the interior of the bladder and prostatic urethra form a continuous pear-shaped cavity. The adjacent skin of the abdomen, thighs, and scrotum is often excoriated and infected from continuous soaking with urine.

The generally accepted embryologic explanation for the occurrence of epispadias and exstrophy of the bladder^{3, 5, 6} is that there is a "cephalad displacement of the cloacal membrane in an early stage of development before the genital tubercle has made its appearance. The genital tubercle developing later arises below the cloacal membrane so that when the membrane is resorbed the urogenital sinus opens on the dorsum of the penis rather than on the ventrum. If the displacement of the cloacal membrane extends on to the primitive abdominal wall the result will be exstrophy of the bladder. If the displacement is of lesser degree epispadias alone results."

Two factors in the treatment of epispadias with incontinence must be considered, namely, correction of the urethral defect and cure of the urinary incontinence. The earliest surgical operations for this condition were directed toward the urethral defect. Thiersch,⁷ in 1869, by means of skin flaps taken from adjacent tissues of the penis, scrotum, and pubis, was able to construct a urethra extending to the end of the penis and by application of a mechanical device which compressed the newly constructed urethra could produce artificial urinary control. This method was only partially successful due to the frequent formation of urethral fistulas. Cantwell,⁸ in 1895, described his operation, which, modified, remains the operation of choice today for construction of the urethra. He noted the ease with which the corpora cavernosa could be separated in cases of epispadias. Utilizing the skin and mucous membrane of the dorsum of the penis he constructed a continuous urethral tube from the retropubic infundibulum to the tip of the penis. The corpora were then separated and the newly constructed urethra displaced to its proper position on the under surface

of the penis and held there by reapproximating the corpora dorsal to it. This procedure succeeded in creating almost normal relationship between the corpora cavernosa and the urethra, its greatest drawback being that sloughing of the newly constructed urethra occasionally occurred because of inadequate blood supply.

In 1918, Young⁹ published his modification of the Cantwell operation which endeavored to avoid ischemia of the newly created urethra. The urethra was constructed from the skin of the dorsum of the penis, but left attached to one corpus cavernosum. After separating the corpora, the one to which the urethra was attached was rotated medially 180 degrees so as to carry the urethra to the under surface of the penis with its vascular connections to the rotated corpus still intact. Successful urethral constructions have also been reported by Barney,¹⁰ Rokey,¹¹ and Cabot,¹² utilizing skin flaps from the prepuce, suprapubic region, or scrotum.

The experiences of these surgeons clearly established two points. Diversion of the urine, either by perineal urethrostomy, or preferably, by suprapubic cystostomy, is imperative for successful healing of the newly constructed urethra. If there is infection or excoriation of the skin of the penis, adequate time for its healing must be allowed after diversion of the urine before construction of the urethra is carried out. Secondly, the "splay" deformity of the penis must be corrected by resection of a portion of the dorsal skin and subcutaneous tissue and approximation by suture of the separated corpora.

Practically all the above authors noticed some degree of improvement in urinary control following simple construction of the urethra, although no correction of the sphincteric defect had been attempted. Page¹³ and Bullitt¹⁴ each reported a case of complete cure of urinary incontinence after simple construction of the urethra by Cantwell's technique. Some have stated that following construction of the urethra, if the sphincters are not too widely dilated, routine "sphincter exercise" may be sufficient to establish some degree of urinary control.

Dnplay,¹⁵ in 1880, recognized that the urinary incontinence in epispadias was due to a defect in the circular muscle fibers of the bladder neck. • He cured one case of incontinence and greatly improved a second by partial resection of the dilated bladder neck and apposition of the cut edges by suture. Boiffin,¹⁶ in 1895, after dissections on an epispadiac cadaver, pointed out that the defect in the internal sphincter was mainly in its anterior portion, and that adequate muscle for urinary control was present in these cases if it could be united. He stressed the importance of removing the anterior defective portion of the sphincters rather than the posterior segment which contained the bulk of sphincteric muscle and reported one case successfully cured of incontinence.

*In female epispadias, plication, with or without torsion of the urethra, has been carried out with rather indifferent success, although Gautier²⁷

reports cure of two cases by this technique. Muscles from other portions of the body have been transplanted and utilized for an artificial urethral sphincter by Deming,¹⁷ Thompson,¹⁸ and others. The gracilis, pyramidalis, rectus abdominis, and gluteus muscles have all been used for this purpose, a few cases of incontinence having been cured by each of these procedures.

In 1906, Trendelenberg¹⁹ advocated excision of a broad, wedge-shaped portion of the anterior and lateral walls of the infundibulum from below, reuniting the defect with sutures. If incontinence persisted he operated again and excised more of the urethra and external sphincter. If the infundibulum were very large with some protrusion of the bladder wall through it, he divided the intersymphysial ligament and resected the roof and lateral walls of the prostatic urethra as well as a portion of the bladder neck, reapproximating these structures with sutures. He stressed the importance of reuniting the symphysis pubis with buried silver wire sutures and reported cures of incontinence in two cases.

In 1922, Young²⁰ described his double sphincter operation for the cure of epispadias with incontinence. The details of this operation are well known and consist of suprapubic cystotomy with excision of an appropriately large wedge-shaped piece of tissue from the roof of the prostatic urethra and the anterior portion of the vesical orifice. The cut edges are reapproximated by means of continuous suture, so as to draw together and tighten the prostatic urethra and internal vesical sphincter. The intersymphysial band is not divided but the roof and a portion of the lateral walls of the infundibulum and the anterior portion of the external sphincter are excised from below. These raw edges are likewise reapproximated by continuous suture, thus tightening the external sphincter and bulb of the urethra. In 1940, Dr. Young²¹ reported thirteen cases of epispadias with incontinence on whom this operation had been performed with creation of complete urinary control in twelve cases and almost perfect control in the other. Mueschat,²² in 1927, reported three cases of epispadias with incontinence cured by Young's operation. Other cures have been reported by Cecil,²³ Lowsley and Kirwin,²⁴ Hinman,¹ and others.

Exstrophy of the bladder at the present time is usually treated by transplantation of the ureters into the sigmoid. Some^{25, 26} have advocated this as the procedure of choice in epispadias with incontinence. Others have resorted to its use only after plastic operations on the vesical sphincters have failed.

Since the opening of the Duke Hospital five patients with epispadias have been seen, three of whom had complete urinary incontinence. One of these three patients refused operation. The other two patients were operated upon and excellent results were obtained.

CASE 1 (Duke Hospital No. 59615).—H. R. S., a 14-year-old white boy, was admitted on the Urological Service, Oct. 15, 1935, complaining of urinary incontinence.

tinence and deformity of the penis since birth. The past health had been excellent. There had been occasional excoriation and infection of the skin around the genitalia but nothing to suggest upper urinary tract infection; erections had been frequent. When the patient was at the age of two or three years, his physician had removed a portion of the prepuce without influencing the urinary incontinence. At the time of admittance he was in the seventh grade of school. He wore cotton pads to protect his clothes from the dribbling urine; although there was constant dribbling, on occasions the child would void a considerable amount, varying from 50 to 100 c.c. but immediately afterward urinary dribbling would continue.

General physical examination was negative except for a well compensated rheumatic heart disease. The penis presented a classical picture of complete epispadias with incontinence (Fig. 1), measuring 4 cm. in length and being broad and thick. Urine constantly seeped from the retropubic infundibulum. Intra venous urograms and plain x ray showed a normal upper urinary tract and some separation of the symphysis pubis.



Fig 1 (Case 1) —Epispadias with incontinence, appearance of penis before and after operation.

On Oct. 23, 1935, the bladder was opened suprapubically and found to be large and atonic. The internal sphincter was relaxed. Young's double sphincter operation was carried out in two stages, the repair of the internal vesical sphincter being done at this time and construction of the urethra carried out, Dec. 2, 1935. Convalescence from both procedures was uneventful, the urethral repair healing per primam. The patient was discharged Jan. 25, 1936, voiding normally from the new urethral meatus without incontinence. On Sept. 8, 1941, almost six years after operation, the patient reported by letter that he was doing heavy manual labor and that urinary control was perfect.

CASE 2 (Duke Hospital No. A57641).—J. E. B., a 15 year old boy, was admitted on the Urological Service, March 11, 1941, complaining of deformity of the penis and constant dribbling of urine since birth. No attempts at surgical correction

of the deformity had been made, nor had any apparatus or dressing been used to collect the urine. The boy had never been to school and was shunned by other children. There was nothing in the past history to suggest upper urinary tract infection. Occasionally there had been fairly firm erection, but there was no history of ejaculation or orgasm.

Examination disclosed a tall, shy, undernourished boy of fifteen. His clothing below the waist was soaked with malodorous urine. Over the thighs and lower abdomen were numerous furuncles. The penis showed complete epispadias with incontinence (Fig. 2) and the examiner's finger could easily be passed through the infundibulum into the bladder. The corpora cavernosa were easily separable along the proximal half of the shaft of the penis, distal to which point they were firmly attached together. At the summit of the glans was a small dimple, through which, on subsequent investigation, sounds could be passed into a false urethra along the under surface of the corpora. This terminated blindly beneath the



Fig. 2 (Case 2).—Epispadias with incontinence; appearance of penis before and after operation.

mucous membrane covering the dorsal groove of the penis just proximal to the point of separation of the corpora. Both testicles were descended and of normal size. Rectal examination disclosed a prostate of average size for a 15 year-old boy. On cystoscopy the bladder wall was normal, the bladder capacity being 130 c.c. There was no evidence of cystitis. The trigone was indistinct and difficult to delineate. With very little fluid in the bladder, a relaxed internal vesical sphincter could be visualized, but on partially filling the bladder this region was completely smoothed out, the bladder wall appearing continuous with the prostatic urethra. The verumontanum was prominent and both the utricle and left ejaculatory duct were easily seen. No definite external urethral sphincter could be demonstrated. Plain x-ray and intravenous urograms showed a normal upper urinary tract. The urine was normal and uninfected.

On March 17, 1941, a modification of Young's operation for epispadias with incontinence was carried out. The procedure differed from Young's classical operation in several technical points which we feel are worthy of recording. The

bladder was exposed by a generous midline incision, but prior to opening, its anterior and lateral walls, as well as the anterior and lateral surfaces of the prostate, were completely freed by blunt dissection down to the triangular ligament. The puboprostatic ligament was easily broken with the dissecting finger. The bladder and prostatic urethra were opened along the midline anteriorly down to the external sphincter. Since the internal vesical sphincter could not be identified as such, a point was arbitrarily chosen halfway between the verumontanum and interureteric ridge for the new bladder neck. A triangular piece of bladder wall and prostate was then removed from each side of the midline (Fig. 3). The incisions were so placed that the base of each triangle was represented by the midline incision through the bladder and prostate and the apices of the triangles lay about 8 mm apart at the level chosen for the internal vesical sphincter. The

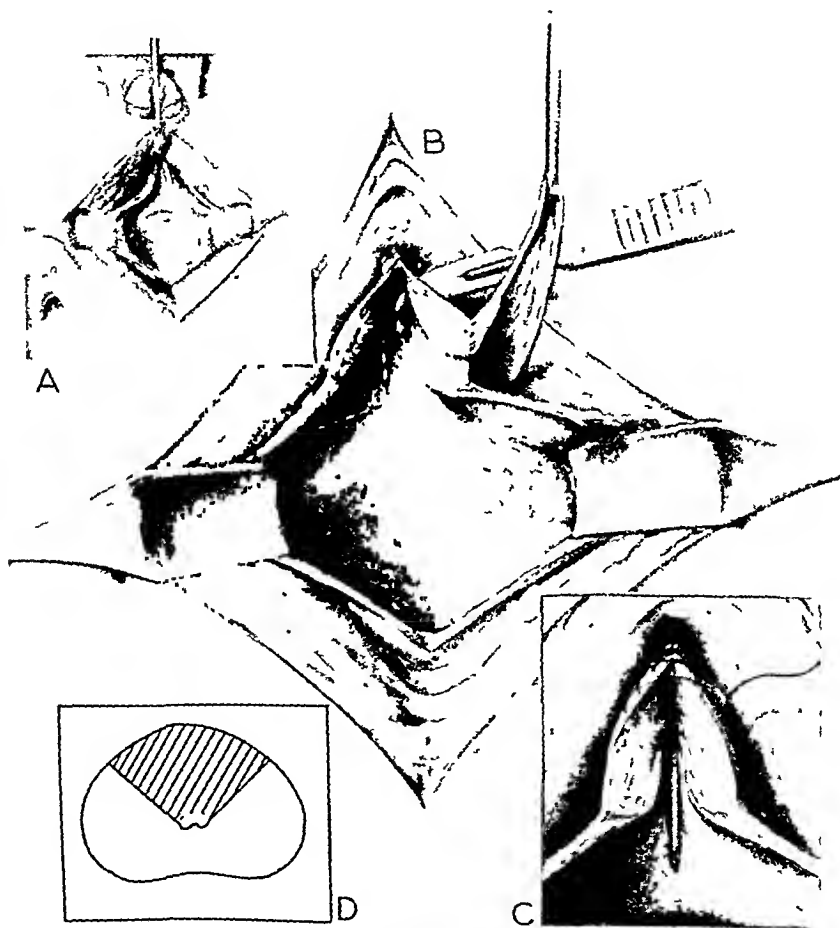


Fig. 3—t. Young's technique for resection of wedges from vesical neck and prostatic urethra. B, Bladder and prostatic urethra opened along midline to membranous prostate, resection of triangular piece of tissue from roof and right lateral lobe of prostate and adjacent bladder, cut edges of floor of prostatic urethra are parallel and corresponding tissue is excised from left side as indicated. C, Closure sutures results in tubular urethra, tight internal sphincter, sec- Closure floor of urethra but of most of lateral prostatic lobes by oblique incisions.

incisions through the prostatic tissue were made obliquely, preserving a strip of mucosa along the floor of the urethra, 8 mm. in width, and the greater portion of the lateral lobes of the prostate. The prostatic urethra was then closed over a No. 8 French soft rubber catheter in two layers, the first layer of sutures snugly approximating the structures, the second layer plicating the prostatic urethra and internal sphincter. The bladder was closed around a mushroom catheter with chromic catgut, the wound closed and drained routinely. The lateral walls and roof of the infundibulum as well as the anterior segment of the external sphincter were then excised from below according to Young's technique. The mucosa and periurethral tissues were closed over the catheter with fine chromic catgut.

Following removal of the suprapubic catheter on the seventeenth day, urinary control was rapidly established and by the thirty-eighth postoperative day was almost perfect. On this date the bladder was reopened and drained suprapubically. A No. 16 sound was introduced into the false urethra and its tip forced through the mucosa covering the dorsal groove of the penis. A relatively short segment of urethra connecting the infundibulum with the proximal end of the false urethra was constructed from the mucous membrane of the dorsum of the penis. After the anastomosis was completed the proximal halves of the corpora were separated, the newly constructed urethra displaced ventral to them and held there by re-approximating the corpora with chromic catgut sutures. A longitudinal segment of skin and fibrous tissue was excised from the dorsum of the distal half of the penis and glans, the defect being closed with vertical mattress sutures of fine silver wire.

Convalescence was uneventful, the urethral construction healing per primum without fistula. At the time of discharge, May 27, 1941, the patient was voiding with perfect urinary control during the day, but having slight incontinence at night while asleep. The operative incisions were completely healed. Five months later the patient could retain urine for more than four hours and had perfect control during both day and night except for very occasional enuresis. Erections had been frequent but intercourse or masturbation had not been attempted. The urine was normal and the urethra easily accommodated a No. 16 French sound.

COMMENT

The embryologic vagary responsible for the concomitant occurrence of epispadias and an essentially normally placed false urethra offers room for speculation. According to Bremer³ and Arey,⁶ the cloacal membrane originally extends from the tail bud to the future umbilical cord. Normally, by the time the genital tubercle has appeared, the cloacal membrane has receded so as to cover only the caudal surface of the tubercle and the perineum forming the urogenital sinus which later closes to form the urethra. Failure of recession of the cloacal membrane from the lower abdomen or ventral surface of the genital tubercle results in exstrophy of the bladder or in epispadias. In our case, it seems probable that there was a separation of the cloacal membrane into two portions, one dorsal and one ventral to the crest of the genital tubercle, the former resulting in epispadias and the latter forming the terminal portion of the pendulous urethra. It is interesting to note that the corpora cavernosa were firmly attached together along that segment of the penis traversed by the false but normally located urethra, whereas proximal to the false urethra they were considerably separated.

DISCUSSION

There is, of course, no way of accurately estimating the percentage of cure of epispadias with incontinence by plastic operation on the vesical sphincters and urethra. The operative result, naturally, will be governed by the operative technique employed, the surgeon himself, the amount of sphincteric muscle available for approximation, wound infection, and a host of other factors. As with many surgical procedures, operative failures are much less frequently reported than are successes. It seems significant, however, that in all reported groups of cases, almost without exception, the urinary incontinence was either completely cured or very greatly improved after partial resection and reapproximation of the vesical sphincters. If the outcome of operation is successful, these individuals are restored to a completely normal social state and to a practically normal physical condition. Coitus is usually quite satisfactory, moderate upward curvature of the penis being much less of a handicap than a corresponding degree of ventral chordee. Urinary infection, if present, presents no different therapeutic problem than it does in a normal individual. The upper urinary tract has not been disturbed and the life expectancy of the individual should not differ from the average at his age. This is in distinct contrast to the conditions obtaining after ureteroenterostomy, where chronic renal infection is almost the rule. The great value of ureteral transplantation to the bowel is unquestioned in certain incurable conditions, such as exstrophy of the bladder, and vesical carcinoma. In epispadias with incontinence, however, where the abnormality is curable in a fairly high percentage of the cases, we feel that the advantages of plastic repair so far outweigh those of ureteroenterostomy that the latter should be reserved as a procedure of last resort.

REFERENCES

1. Hinman, Frank: *The Principles and Practice of Urology*, Philadelphia, 1935, W. B. Saunders Company.
2. Nove-Josserand, G.: *Traitement de l'hypospadias: Nouvelle methode*, Lyon méd. 85: 198, 1897.
3. Bremer, J. L.: *Hypospadias and Epispadias: A Philological Note*, New England J. Med. 207: 537, 1932.
4. Thompson, A. R.: *Clinical Anatomy of Cases of Epispadias and Extroversion of Bladder*, Brit. J. Child. Dis. 35: 36, 1938.
5. Johnson, F. P.: *Young's Practice of Urology*, Philadelphia, 1926, W. B. Saunders Company.
6. Arey, L. B.: *Developmental Anatomy*, Philadelphia, 1934, W. B. Saunders Company.
7. Karl Thiersch: *Ueber die Entstehungsweise und operative Behandlung der Epispadie*, Arch. f. d. homöop. Heilk. 10: 20, 1869.
8. Cantwell, F. V.: *Operative Treatment of Epispadias by Transplantation of Urethra*, Am. J. Surg. 22: 689, 1925.
9. Young, H. H.: *A New Operation for Epispadias*, J. Urol. 2: 237, 1918.
10. Barney, J. D.: *Epispadias*, Surg., Gynec. & Obst. 23: 594, 1916.
11. Roockey, E. W.: *Repair of Epispadias and Exstrophy of Bladder*, S. Clin. North America 8: 1502, 1928.
12. Cabot, H.: *Plastic Operations for Epispadias, Hypospadias and Urethral Stricture*, Proc. Staff Meet., Mayo Clin. 5: 315, 1930.
13. Page, H. W.: *Cantwell's Operation for Epispadias*, The Lancet 2: 1193, 1898.

incisions through the prostatic tissue were made obliquely, preserving a strip of mucosa along the floor of the urethra, 8 mm. in width, and the greater portion of the lateral lobes of the prostate. The prostatic urethra was then closed over a No. 8 French soft rubber catheter in two layers, the first layer of sutures snugly approximating the structures, the second layer plicating the prostatic urethra and internal sphincter. The bladder was closed around a mushroom catheter with chromic catgut, the wound closed and drained routinely. The lateral walls and roof of the infundibulum as well as the anterior segment of the external sphincter were then excised from below according to Young's technique. The mucosa and periurethral tissues were closed over the catheter with fine chromic catgut.

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A NEW SKIN VARNISH FOR MAINTAINING STERILITY OF THE OPERATIVE FIELD

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ALTHOUGH avoidable infections of operative wounds may be expected to take place as long as operations are performed, surgeons will always strive to minimize them. The percentage of infections in clean surgical wounds is still significant.¹ This paper is not concerned with bacteria which may be in the air, on contaminated instruments, or on the hands of the surgical personnel but only those on the skin of the operative field.

It has been abundantly demonstrated that the tissues surrounding a wound cannot be completely sterilized by any methods now in use. Bacteria which remain deep in the sweat and sebaceous glands are washed out with perspiration and are readily swept into wounds by instruments or the hands of the surgeon.² Because of this danger, many surgeons protect the edges of the wound with skin towels through which, however, perspiration or other fluids may soak. Some surgeons apply antiseptics or bacteriostatic agents just before closing the wound. It is debatable what percentage of wound infections can properly be ascribed to contamination with organisms from the contiguous skin but proper provision should be made to minimize this risk.

Rubber gloves³ are worn almost universally now to protect the wound from bacteria on the surgeon's hands. Since it is just as impossible adequately to sterilize the human abdomen as it is to sterilize the human hand,⁴ there have been many attempts to isolate the operative field by means of impervious materials, such as silk dipped in collodion,⁵ rubber sheets, and various waxes.^{5, 6} None of these methods has come into general use.

Accordingly, a preparation has been devised at my request by Mr. Carl Bauer, a research chemist. This substance is a cellulose product which is dissolved in a mixture of ether and alcohol and is referred to as skin varnish.* It is self-sterilizing and can be sprayed or painted on the skin of the operative field forming an impervious coating which is insoluble to water but which, unlike collodion, can easily be redissolved at the end of the operative procedure. This preparation is

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*The skin varnish, known as Surgical Skin Varnish, is available for investigational use on application to E. R. Squibb & Sons. The formula is as follows: ethyl cellulose, 165.0 Gr.; acetone, 605.0 Gr.; ethyl alcohol, 715.0 Gr.; butyl lactate, 22.0 Gr.; castor oil, 16.5 Gr.; and sanitizer B-16 (Monsanto), 16.5 Gr.

14. Bullitt, J. B.: *Epispadias*, J. A. M. A. 41: 297, 1904.
15. Duplay, S.: Sur le traitement Chirurgical de l'hypospadias et de l'epispadias, Bull. et mém. Soc. de chir. de Par. 6: 169, 1880.
16. Boiffin, A.: Epispadias complete penopubien; reconstruction du col de la vessie apres symphysiotomie, A. franc. de chir. Proc verb, Par. 9: 576, 1895.
17. Denning, C. L.: Epispadias in Female; Transplantation of Gracilis Muscle for Incontinence of Urine, J. A. M. A. 86: 822, 1926.
18. Thompson, A. R.: Case of Epispadias Associated With Complete Incontinence Treated by Rectus Transplantation, Brit. J. Child. Dis 20: 146, 1923.
19. Trendelenberg, F.: The Treatment of Ectopia Vesiculi, Ann. Surg. 44: 281, 1906.
20. Young, H. H.: An Operation for the Cure of Incontinence Associated With Epispadias, J. Urol. 7: 1, 1922.
21. Young, H. H.: Genital Abnormalities, Hermaphroditism, and Related Adrenal Diseases, Baltimore, 1940, Williams & Wilkins Company.
22. Muschat, M.: Case of Complete Epispadias Associated With Incontinence of Urine Cured by Operation; Four Additional Cases, J. Urol. 18: 177, 1927.
23. Cecil, H.: Congenital Malformation of the Penis, Cabot's Modern Urology, Philadelphia, 1936, Lea and Febiger.
24. Lowsley, O. S., and Kirwin, T. J.: Clinical Urology, Baltimore, 1940, Williams & Wilkins Company.
25. Walters, W., and Brausch, W. F.: Ureteral Transplantation to Rectosigmoid for Ectrophy of Bladder, Complete Epispadias, and Other Urethral Abnormalities With Total Urinary Incontinence, Am. J. Surg. 23: 255, 1934.
26. Ladd, W. E., and Lanman, T. H.: Ectrophy of the Bladder and Epispadias, New England J. Med 222: 130, 1940.
27. Gautier, J.: Traitement des Incontinences graves d'origine urétrale par la plicature vésico urétrale, J. d'urol. 44: 55, 1937.

when both iodine and varnish were used. Under these circumstances, eleven of seventeen cases were completely sterile and there were never more than six colonies per watch glass.

In the skin that was only cleansed there were four instances in which more than 100 colonies were present but in the other thirteen instances there were never more than ten colonies. When iodine alone was used there were two cases of the seventeen where two hundred colonies were found. However, when the varnish was used with or without iodine there were never more than ten colonies per watch glass. These observations suggest that it is only the occasional patient who has a significant number of organisms in the depths of the sweat and sebaceous glands of the abdominal wall. These patients may be especially likely to suffer from wound infection.

CLINICAL RESULTS

The varnish has been used in forty major operations since July 9, 1940. There were seven laparotomies, sixteen laminectomies, and seventeen craniotomies. The skin was usually prepared with soap and water, ether, alcohol, and iodine. In one case the patient was sensitive to iodine and merthiolate was used as the antiseptic agent. The varnish was applied with a sterile sponge or with an atomizer* so that a thin coating lay on the skin of the operative field. If wound towels were used in addition to the coating and were rubbed firmly over the skin, the varnish was scraped off. Otherwise, the coating was intact at the end of the procedure, when the varnish was removed with a mixture of alcohol and ether.

In no case was there irritation of the skin or any interference with healing of the wound. There were two cases of low-grade infection of the wound following removal of a gangrenous appendix, and one following an umbilical hernioplasty. There was one wound infection following hemilaminectomy in a man 73 years of age. The other thirty-six wounds healed by primary intention. The percentage of infection in these cases is without significance because suitable controls were not available.

Other possible uses of this product, perhaps combined with sulfonamide drugs, in the treatment of burns or chronic ulcers of the skin, and in protecting the skin from noxious discharges and chemical agents should be investigated. It has been used with encouraging results on a persistent bed sore. Because it can be redissolved so easily it may prove to be superior to collodion for many other uses.

CONCLUSION

A new skin varnish fills a theoretic need for preserving sterility of the skin in the operative field. Its value has been confirmed by counts of bacteria on the human abdominal skin under conditions similar to

*The atomizer was supplied by the deVilbiss Co., Toledo, Ohio, and is similar to that used to spray tannic acid.

chemically inert and does not react with iodine or other common antiseptics. The solute is noninflammable, nontoxic, nonexplosive, non-irritating, and does not interfere with healing of wounds or with making an incision. It merely provides an impermeable, pliable, transparent coating over the skin of the operative field which prevents organisms in the skin excretions from being wiped into the wound.

LABORATORY RESULTS*

Bacterial cultures of the varnish in both aerobic and anaerobic media revealed no growth of organisms.

Seventeen male patients on the medical wards of the Syracuse University Hospital were used in testing the preparation in the following manner (a modification of the method of Novak and Hall⁷). Sterile watch glasses containing a nutrient blood agar medium were strapped with the medium next to the unprepared skin of the four abdominal quadrants and allowed to remain for fifteen minutes. These were then removed and incubated for twenty-four hours at 37° C. and the colonies of microorganisms identified and counted. Immediately following the removal of these watch glasses the entire abdomen was shaved, scrubbed for ten minutes with surgical soap, washed with 70 per cent alcohol (by weight) and ether. The two lower quadrants then received two applications of 1 per cent iodine, which was allowed to dry and then removed with 70 per cent alcohol. The two quadrants on the patient's right side were then sprayed with the varnish, approximately 5 to 8 c.c. being used for each case. After the varnish dried, a matter of one or two minutes, the bacteriologic medium was applied to the skin of each of the four abdominal quadrants as previously described. A cradle containing four 40-watt electric light bulbs was placed over the abdomen, the bed clothes were drawn over this and allowed to remain for forty-five minutes. Marked perspiration occurred in each case. The watch glasses were then removed, incubated, the bacteria identified, and the colonies counted. Thus, of the four abdominal quadrants all of which were cleansed with soap, alcohol, and ether, one quadrant was a control, one received only iodine, one only varnish, and one both iodine and varnish before being subjected to heat.

The unprepared abdomen contained a minimum of 260 colonies and an average of 1,231 colonies per watch glass (an area of 33.1 sq. cm.), and there were about the same number of organisms in each quadrant of any given abdomen. The most common organisms were the *Staphylococcus albus* and diphtheroid bacilli. The abdominal quadrant that was only cleansed before being exposed to heat contained an average of seventy-seven colonies per watch glass. The use of iodine, varnish, or both resulted in there being, respectively, an average of twenty-five, three, or one colony per watch glass. Thus, the best results were obtained

*The laboratory studies were carried out by Ralph W. Getty, under the direction of Dr. O. D. Chapman.

A CONSIDERATION OF THERAPY IN STAPHYLOCOCCUS INFECTIONS

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SOME of the most important factors in any consideration of therapy in staphylococcal infections are first, the variations in the bacteria; second, the influence of extrinsic factors on the organism; and third, the dual nature of some staphylococci. There are some staphylococci that show many toxigenic activities similar to those of the diphtheria bacilli and also, the invasive characteristics of certain streptococci. Each of these factors deserves consideration from a therapeutic standpoint.

Reviews recently published discuss many of the characteristics of the staphylococci. Among these is one by Blair¹ in which he reviews the problem of the pathogenic staphylococci. In this he considers the toxin, the coagulase, and the fibrinolytic properties of the staphylococcus. The differentiation of the pathogenic from the nonpathogenic staphylococci is discussed, and the classification of these organisms based upon the agglutinin and precipitin reactions. Blair¹ concludes that "the past several years have witnessed definite advances in knowledge of the staphylococci particularly with regard to their soluble toxic substances. . . . The exact relation of the toxins to the pathogenesis of staphylococcal infections demands further study."

Chapman and his associates,² in a paper entitled "The Differentiation of Pathogenic Staphylococci from Nonpathogenic Types," discuss in detail the various laboratory procedures used in the study of staphylococci, such as pigment production, hemolysis, coagulase, and the fermentation reactions. These investigators emphasize the difficulties that may arise in any study of staphylococci resulting from the development of variants in the cultures. They conclude that "the coagulase test is the most reliable single test for the differentiation of pathogenic from nonpathogenic staphylococci. When used in conjunction with pigment and coagulase tests, hemolysis of rabbit blood agar permits simple estimation of the degree of pathogenicity of a strain or variant." In view of the simplicity of technique by which hemolysis may be studied on rabbit blood agar media as compared with the technique for the coagulase test it would appear that the former test would be of greater value in the separation of pathogenic from nonpathogenic staphylococci.

Flaum,³ in 1938, while reviewing the entire problem of the staphylococcus, considered at length that of immunity. He states that "in recent years the therapy of staphylococcus infections has been taken up with

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those of laparotomy. The varnish does not delay the operation, irritate the skin, or interfere with wound healing. It will not be possible to judge the practical value of this preparation in preventing postoperative infection until it is used in a large number of operations with suitable controls. It is in the hope that such investigations will be carried out in some of the larger surgical clinics that this preliminary report is presented.

REFERENCES

1. Meleney, Frank L.: Infection in Clean Operative Wounds; A Nine-Year Study, *Surg., Gynec. & Obst.* 60: 264-276, 1935.
2. Beck, W. C.: Preparation of Operative Field; Report of Survey of Seventeen Surgical Teaching Clinics, *Arch. Surg.* 33: 876-889, 1936.
3. Halsted, W. S.: Ligature and Suture Material, *J. A. M. A.* 60: 1119-1126, 1913.
4. Maes, N., and Boyce, F. F.: Aseptic Ritual and the Surgeon, *Mod. Hosp.* 40: 41-45, 1933.
5. Küttner, H.: Disinfection of the Hands and Site of Operation, *Ann. Surg.* 55: 129-133, 1912.
6. McDonald, Ellice: A Skin Varnish and Substitute for Rubber Gloves, *M. Rec.* 85: 524-525, 1914.
7. Novak, M., and Hall, H.: A Method for Determining Efficiency of Pre-operative Skin Sterilization, *SURGERY* 5: 560-566, 1939.
8. DeBakey, Michael, Giles, E. J., and Honold, Edith: The Protection of the Operative Field With an Impermeable Adhesive Skin Coating, *Surg., Gynec. & Obst.* 74: 499-504, 1942.

ylcocci. It is important to remember, however, that the red blood cells from different species are lysed at different rates by staphylococci. Gross⁸ gives the order of susceptibility of the red blood cells from different species to staphylococcus toxin as follows: rabbit, ox, sheep, goat, man, guinea pig, and horse. One of us (R. H. R.) has observed a similar order of susceptibility of red blood cells to staphylococcus toxin: rabbit, goat, cow, cat, pig, rat, dog, mouse, monkey, turtle, sheep, man, horse, chicken, and guinea pig. In view of these observations it is important to know the type of red cell used in any blood agar media since the presence of a zone of hemolysis around staphylococcus colonies is considered to indicate a more virulent organism than a strain of staphylococcus that fails to produce hemolysis.

Antitoxin may be one of the factors in blood agar media that accounts for the failure in the development of this hemolytic zone about the colonies of hemolytic staphylococci. Staphylococcus antitoxin added to blood agar media inhibits the hemolysis produced by hemolytic staphylococci growing on the surface of the same plates.⁹ This in vitro demonstration of the neutralization of the toxin by the antitoxin would suggest that a similar effect might occur in vivo.

Hemolysis is only one of the destructive processes resulting from staphylococcus toxin. De Christmas,¹⁰ in 1888, demonstrated the necrotizing action of this toxin on the skin of laboratory animals. More recently pathologic changes in man have been attributed to staphylococcus toxin. Extensive necrosis of the mucosa in the lower ileum and first portion of the colon has been observed in a child dying with a staphylococcus septicemia. The primary infection in this case was in the middle ear and the organism was hemolytic. This intestinal lesion was attributed to staphylococcus toxin since a similar lesion was reproduced in the rabbit's colon by the intravenous injection of staphylococcus toxin.¹¹ Tubular and glomerular lesions also have been observed in cases of staphylococcal infection in man and similar lesions have been produced with toxin in experimental animals.^{12, 13} Fig. 1 illustrates the necrotizing process that may be associated with the development of staphylococcal abscesses in the heart in cases of septicemia. Acute necrotizing ulcers in the skin have been attributed to the action of toxin liberated by the staphylococcus since a toxin producing organism was isolated from the lesions.¹⁴ Pathologic lesions resulting from staphylococci have been described in cases of cavernous sinus thrombosis. The similarity of this lesion to that occurring in the small blood vessels of the rabbit's ear following the intravenous injection of staphylococcus toxin was demonstrated by Stookey and Scarpellino.¹⁵ The coagulation of the tissue that may follow the local injection of staphylococcal toxin in experimental animals resembles the lesions that may occur in certain of the viscera following the intravenous injection of the same filtrate. The degree of injury may be influenced by the type of cell and con-

greater eagerness and enthusiasm perhaps than ever before and results have been published by various workers which seem to justify the enthusiasm with which they have been made known. The new feature of the methods which have been brought into use is that staphylococcal toxin as a rule in the form of toxoid, and serum, containing staphylococcal antitoxin, constitute the new weapons in the therapeutic arsenal, the purpose of which is to produce an active or passive immunity against staphylococci and their products."

Rigdon,⁴ in 1937, reviewed the problems of staphylococcal immunity in both man and experimental animals. From this paper there appears to be unquestionable evidence to indicate that staphylococcal antitoxin antibodies may play a very important role in the mechanism of the resistance of both man and experimental animals to staphylococcal infections. Staphylococcal toxoid would appear to be the antigen of choice in the immunologic treatment of skin infections. Staphylococcal antitoxin is of value in the treatment of certain acute cases of staphylococcal infections, especially those in which the clinical manifestations of toxemia are greater than one would expect from the number of bacteria present in the blood stream.

In a second review on staphylococcus toxin Rigdon⁵ points out that evidence from the literature indicates that the toxin produced by certain staphylococci consists of a single toxic substance. There is insufficient data, he thinks, to prove that the lysis of red cells, the necrosis of epithelial cells in the skin, the destruction of white blood cells in the circulating blood, and the development of renal necrosis following an intravenous injection of staphylococcus toxin are the result of the action of four different toxic substances, each given off by the organism in the same preparation of filtrate. Rigdon considers that each of these pathologic lesions represents only a variation in the effect of a single substance reacting upon different tissues. If this concept is correct, then the use of one antitoxin would suffice to neutralize all the different effects produced by staphylococcus toxin. Rigdon has demonstrated that each of the so-called "fractions" in staphylococcus toxin was destroyed by the same agents. In these experiments the toxin was detoxified by several different methods and in each the hemolysin decreased at a rate comparable to the rate of destruction of the so-called "skin necrotizing factor."^{6, 7}

The frequency in which studies on staphylococci are being published would indicate a growing interest in the morbidity and the mortality of such diseases as osteomyelitis, skin infections, food poisonings, and septicemia. They also indicate the need for diligent investigation of the staphylococcus and the therapy to combat it.

A simple technique for the classification of staphylococci would be valuable in any consideration of therapy. Blood agar media may contribute much in the separation of pathogenic and nonpathogenic staph-

organism is present that will neutralize the toxin liberated by the bacteria. Experimental and clinical studies have been made to study the effect of staphylococcus antitoxin on the lesions produced by different strains of staphylococci and staphylococcal toxin.¹⁶⁻²³ This antitoxin when given to rabbits prevents the acute death that follows the intravenous injection of staphylococcal toxin. The histologic reaction that occurs in the subcutaneous tissue of mice following the local injection of a toxin-producing strain of staphylococci is essentially the same as that which occurs when a nontoxin-producing strain of staphylococci is injected subcutaneously if the animals are given staphylococcus antitoxin preceding the injection of the bacteria.¹⁶

Staphylococcus antitoxin and the results of its clinical use in the treatment of staphylococcal infections apparently was satisfactory, for the Council on Pharmacy and Chemistry of the American Medical Association accepted it in August of 1940.²⁵ The following two cases illustrate the use of staphylococcus antitoxin in the treatment of staphylococcal septicemia.

CASE 1.—A 4 year old white female entered the hospital on July 20, 1939, with vesicular blebs over her neck, face, and scalp. These varied in size from 0.5 to 1.5 cm. in diameter and were 0.5 cm. in height. They were filled with a clear amber colored serous fluid, cultures from these blebs showed a hemolytic *Staph. aureus*. A blood culture taken on the second day of hospitalization was also positive for a hemolytic staphylococcus. It showed both aureus and albus colonies. A third blood culture taken on the seventh day of hospitalization, however, was sterile after seven days of incubation.

The temperature, pulse, and respirations for the six days following admission are shown in Fig. 2. The child, on the fourth hospital day, was given 100,000 units of staphylococcal antitoxin intramuscularly over a period of ten hours. An additional intramuscular injection of 20,000 units of antitoxin was given on the fifth day. The child was much improved on the sixth day. A small transfusion was given at this time, the temperature was 101° F. She continued to improve and was dismissed on the twenty fifth day of hospitalization.

CASE 2.—E. P. A 23 year old white female observed that her breasts were sore following the nursing of her baby. When she entered the hospital the right breast was very tender and the upper outer quadrant was firm. She had a severe chill and a rise in temperature during the evening of her first day in the hospital. A blood culture taken at this time was positive for a hemolytic *Staph. albus*. Ten grams of sulfanilamide were given to her on the second day of hospitalization. On the third day 50,000 units of staphylococcus antitoxin were given in 800 c.c. of a 10 per cent solution of glucose. This amount of antitoxin was repeated twenty four hours later.

The patient felt much better on the fourth day. A blood culture taken at this time was sterile after seven days of incubation. A serum reaction occurred on the ninth day following the injection of the antitoxin. The patient improved and was discharged on the fifteenth day following hospitalization.

The dose of staphylococcus antitoxin always should be an amount sufficient to produce an excess of antitoxin in the circulating blood. The minimum dose should be 100,000 units preferably given intravenously.

centration of the toxin in the cells. The union of the toxin with the cell apparently is rapid and irreversible. In all pathologic conditions in which the staphylococcus is the etiologic agent, toxin may account for a considerable part of the clinical and pathological picture.¹⁴



Fig. 1.—The cardiac muscle surrounding the abscess; necrosis may be classified as coagulation necrosis; thus experimentally by staphylococcus toxin. The patient, a male, had a *Staphylococcus aureus* septicemia.

The type of
produced
male, had

The pathologic changes that occur in the subcutaneous tissue of mice are different following the subcutaneous injection of toxin and nontoxin-producing strains of staphylococci. In the former there is a diffuse spread of the bacteria and extensive necrosis; in the latter there is essentially no necrosis and complete localization of the bacteria after a period of approximately eight hours.¹⁶ These observations on the effect of toxin and nontoxin-producing strains of staphylococci on tissue indicate that toxin is one factor that must be remembered in considering therapy in all cases of staphylococcal infections.

STAPHYLOCOCCUS ANTITOXIN

It would appear only logical to consider the use of a therapeutic agent in those cases of staphylococcal infections in which a toxin-producing

CHEMOTHERAPY

There is the problem of the effects produced by staphylococci per se on the tissues of the body in addition to the action of the toxin. Some cultures of staphylococci do not produce toxin in vitro, and furthermore, should the toxin be neutralized in vivo, the bacteria remain. The result of the many experiments on phagocytosis, opsonins, agglutinins, increased rate of removal of staphylococci from the blood stream of immune animals, and the "microbic tissue-affinity" have not solved the problem of the morbidity and mortality of staphylococcal infections.

There was some expectation that the problem of the treatment of staphylococcal infections would be solved following the introduction of sulfanilamide. There have been many observations, both experimental and clinical, discussing chemotherapy.²⁷⁻⁴² Farrell,⁴³ in discussing these experimental observations, says, "Only a broad hint as to therapeutic efficiency is gained from these experimental studies."

A knowledge of the action of sulfanilamide and its associated compounds on staphylococcal toxin is important since it has been established both experimentally and clinically that staphylococcal toxin is a factor to be considered in many of the staphylococcal infections. Carpenter and his associates^{44, 45} found that the lethal action of staphylococcal toxin for mice was inhibited when the toxin was mixed with sulfanilamide preceding an intraperitoneal injection but Rigdon and Avery, in unpublished experiments, found that the hemolytic and the skin necrotizing action of staphylococcus toxin was not inhibited by either sulfanilamide or sulfapyridine. Rigdon and Freeman⁴⁶ concluded from their studies that "the hemolytic, the skin necrotizing and the lethal factors in staphylococcus toxin apparently are not affected by sulfapyridine." Baylis⁴⁷ observed that the addition of various dilutions of sulfanilamide, sulfapyridine, and sulfathiazole to a dose of staphylococcus toxin slightly enhances rather than neutralizes the lethal action of the toxin. Furthermore, he has shown that the dermonecrotic toxin, the coagulase, and the enterotoxin are not neutralized by solutions of the sulfanilamide tested at 37.0° C. The experimental results of Baylis,⁴⁷ and Rigdon and Freeman,⁴⁶ would suggest that sulfanilamide and its derivatives effect staphylococci, probably by inhibiting the growth and the multiplication of the organism, thereby indirectly decreasing the production of toxin and not by directly neutralizing any of the toxic substances produced by the bacteria.

The methyl and phenyl thiazole derivatives of sulfanilamide are markedly bacteriostatic for *Staph. aureus*.⁴⁸ In this connection, Rigdon and Freeman⁴⁶ observed that sulfapyridine in extract broth has a bacteriostatic effect upon staphylococci. In these experiments there was observed a considerable variation in the action of this drug upon the different strains of staphylococcus. The strain most susceptible to the

In severe infections with profound toxemia, 300,000 to 400,000 units of antitoxin may be required. This foreign protein is rapidly eliminated from the body. It is usually absent from the blood in five to seven days. Parrish has demonstrated a simple technique for titrating the antitoxin (antihemolysis) in the serum of patients.²⁶ There is no method at this time by which the quantity of staphylococcal toxin in the blood may be determined.

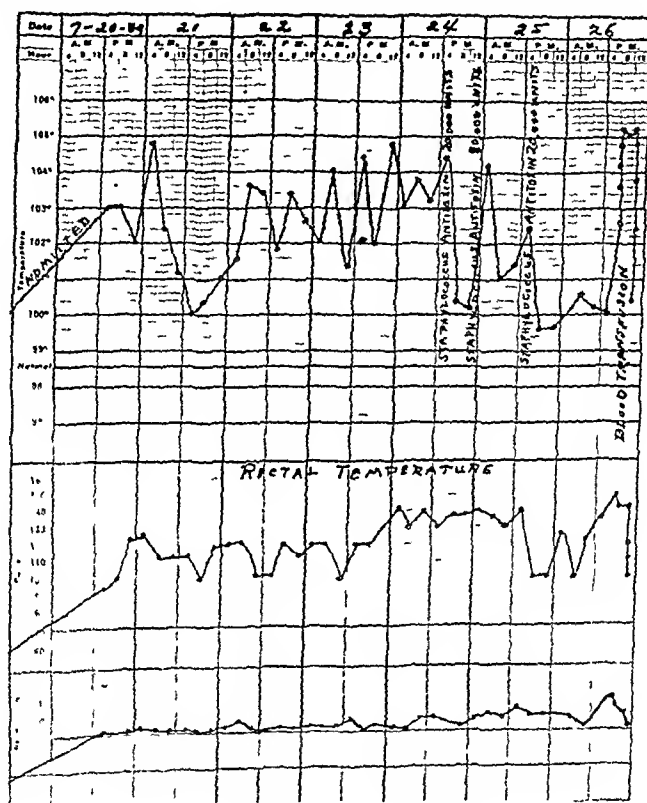


Fig. 2.—The effect of staphylococcus antitoxin on a child 4 years old with a hemolytic *Staphylococcus aureus* septicemia

It has been suggested that staphylococcal antitoxin acts in the following ways: "The toxin produced by the staphylococcus in vivo is neutralized by this antitoxin; a component of the immune serum may act on the staphylococci and increase the ease with which they are phagocytosed by certain organs, especially the liver and spleen. The antitoxin in the circulation may also inhibit the action of leucocidin and thus allow the polymorphonuclear leucocytes to phagocytose the bacteria in either the blood or the tissue."²⁴ If staphylococcus antitoxin acts in this manner, then it may help indirectly in phagocytosis, a process most important in eliminating bacteria from the body.

in the treatment of pneumococcal infections. Long and Haviland⁵⁵ in discussing the problem of pneumonia with reference to chemo- and serotherapy say, "Patients who are severely ill should receive specific serum in addition to either sulfathiazole or sulfapyridine." De and Basu,⁵⁶ in 1938, first suggested that a combination of serum and a chemotherapeutic agent may offer advantages in staphylococcal therapy. Approximately a year later an editorial in the *Lancet*⁵⁷ suggested that "combined chemo- and serotherapy would seem to deserve an extended trial." In August, 1940, a second editorial⁴⁹ in the *Lancet* stated that in septicemia and bacteremia "antisera have gone out of fashion but the antitoxins to both *Staphylococcus aureus* and *Streptococcus pyogenes* should be used in full doses along with chemotherapy in any fulminating septicemia due to these organisms. The sulfonamides have their greatest sphere of usefulness in the prophylaxis of septicemia by localizing an infection already established in the tissues or by preventing infection where there is a strong likelihood of its occurrence." As recent as October, 1940, Farrell⁵⁸ expressed the opinion that "a few unreported clinical trials of combined treatment with antitoxin and sulfapyridine have been strikingly successful." Experimental observations on mice support these clinical observations.^{43, 56, 58}

Goldberg and Bloomenthal,⁵⁹ in April, 1941, reported a series of thirty-two cases of staphylococcal septicemia in which various types of therapy are used. These investigators conclude that "of the various types of therapy employed in any one series, staphylococcus antitoxin and sulfapyridine gave the most direct evidence of favorably influencing the course of the disease." The following case is one included in the paper by Goldberg and Bloomenthal and illustrates the use of chemo- and serotherapy in the treatment of acute staphylococcal septicemia.*

*Case Report (No. 30).—*A 10 year old male had a small carbuncle on his neck for one week prior to his admission to the hospital on Feb. 12, 1939. His temperature was 102.8° F. and the family was told that the fever seemed out of proportion to the size and appearance of the lesion. That afternoon, under ethylene anesthesia, crucial incisions were made and frank pus was evacuated. Cultures of this pus revealed a *Staph. aureus*. In the next twelve hours the patient had three chills and the temperature rose to 104° F. The boy was very toxic; he vomited several times and was irrational at intervals. His leucocyte count was only 6,900. It was thought that he had a fulminating septicemia, probably staphylococci. Blood was drawn for culture and vigorous treatment was instituted. He was given 30 gr. (2 Gm.) of sulfapyridine by rectum every four hours. He received 250 c.c. of blood by indirect transfusion, following which a total of 110,000 units of staphylococcus antitoxin was administered intravenously. The antitoxin was diluted by saline solution and it was given over a period of eight hours. Fifteen minims of adrenalin solution (1:1,000) were given with this foreign serum since the patient was allergic. His temperature reached 106.6° F. that night. It then dropped rapidly to normal and remained there except for a slight transient rise which occurred two days later.

*Permission to include this case and Fig. 3 is granted by Goldberg and Bloomenthal.⁶

action of sulfapyridine was a nontoxic-producing organism. In contrast to this, the two strains of staphylococci most resistant to this drug were both toxin-producing organisms. It will be necessary to make subsequent studies to determine whether there is any correlation between the toxin production and the bacteriostatic resistance of staphylococci to sulfapyridine.⁴⁶

Chemotherapeutic agents now are used almost routinely in the treatment of staphylococcal infections. The clinical results obtained with the different preparations vary. Sulfathiazole, however, appears to be of greater value than sulfanilamide and sulfapyridine in the treatment of staphylococcal infections. An editorial⁴⁹ appearing in the *Lancet* in August, 1940, discussed this problem. It stated that "for staphylococcal septicemia the new sulfathiazole (M & B 760) is recommended (12 to 15 gr. daily). . . . Much has been expected of the sulphonamides and much has been attained, but many patients with staphylococcal . . . septicemia still die despite the new chemotherapy and if progress is to be made our failures as well as our successes should be recorded."

The clinical results following the use of sulfathiazole frequently have been very good. Alya and Roberts⁵⁰ reported cures in six cases of staphylococcal infection in the urinary tract. Helmholz and Larson⁵¹ found sulfathiazole bactericidal for the staphylococci in the urinary tract. A concentration of 300 mg. per 100 c.c. was suggested for the treatment of urinary tract infections.⁵¹ Staphylococcal infections in the meninges also have been successfully treated with sulfathiazole.^{52, 53}

Sulfathiazole has been applied locally in the treatment of certain staphylococcal infections. The preparations used have included sulfathiazole crystals, an aqueous suspension of sulfathiazole used as an irrigant and also for saturating dressings, and sulfathiazole suspended in cod-liver oil. The success of the local use of sulfathiazole, according to Spink and Paine,⁵⁴ is dependent in a great measure upon maintaining a lesion free of purulent and necrotic material. According to these investigators the clinical results obtained so far warrant further investigation of this form of therapy.

The opinion, as expressed by Spink and Paine following the local application of sulfathiazole, apparently may also be made about all the published results of the chemotherapeutic agents used in the treatment of staphylococcal infections. The data at this time apparently are insufficient to evaluate the efficiency of these chemotherapeutic agents; however, in view of the fact that they may be given to patients with only a little likelihood of unfavorable results, it appears to us that their use should be continued.

A COMBINATION OF CHEMOTHERAPY AND SEROTHERAPY

The use of two therapeutic agents simultaneously may not be considered always advisable. Such a combination, however, has been used

The mode of action of staphylococcal bacteriophage is not as obvious as that of staphylococcal antitoxin. Phage is neither a toxin nor an antitoxin.⁶¹ However, Longacre has suggested that the evidence indicates that part of its therapeutic action may depend upon its antigenic properties.⁶⁰

The mortality in cases of acute staphylococcal septicemia treated with phage is surprisingly low as shown by the following data: seven cases treated with one death, a mortality rate of 14.2 per cent.⁶² Longacre,⁶⁰ and Jern and Melency⁶³ report a mortality of 28.5 per cent in a group of twenty-one cases and 73 per cent in a second group of fifteen cases. These authors emphasize, however, the greater potency of the phage used in the treatment of the former group. McNeal and Frisbee report⁶⁴ a mortality of 75 per cent in a group of 100 cases of staphylococcal septicemia treated by the intravenous injection of bacteriophage.

There is some evidence to indicate that phage may increase the leucocytic response of experimental animals to the staphylococcus and probably increase phagocytosis. Until the mechanism of the action of staphylococcus bacteriophage is better understood and the clinical evidence of its efficiency is unequivocal it appears to us at this time that certain therapeutic agents other than phage may prove more efficacious in the treatment of staphylococcus septicemia.

STAPHYLOCOCCUS TOXOID

The treatment of recurrent staphylococcal infections of the skin is frequently a difficult problem. Since the staphylococcus may serve as an antigen it would seem that a person with a recurrent staphylococcal infection should have a higher immune titer than normal individuals. One must remember, however, that the production of immunity is not dependent on the antigen alone but also on the reactivity of the host.

Experimental and clinical observations have been made with both viable and heat-killed staphylococci.⁶⁵⁻⁶⁹ There is a diversity of opinion as to the clinical value of vaccines in the treatment of staphylococcal infections. Klotz and Holman⁷⁰ state that the use of vaccines with killed staphylococci has a long and variable history of great successes and failures.

Burnet,⁷¹ in 1929, was the first to prepare a staphylococcal antigen by detoxifying a staphylococcal filtrate with formaldehyde. This and similarly treated preparations have been studied extensively both experimentally and clinically.⁷²⁻⁷⁵ The Council on Pharmacy and Chemistry accepted staphylococcus toxoid in 1935.⁷⁶

Whitby,⁷⁷ in 1934, treated a group of 100 patients who had localized staphylococcal infections with staphylococcal toxoid and found that it gives more consistent results than any other antigen. He emphasized the fact, however, that patients vary in their response to staphylococcus toxoid. Whitby,⁷⁸ in 1936, again reported his results on a larger series

At this time *Staph. aureus* in pure culture was reported as grown from the blood. Soon after the antitoxin was given the vomiting stopped. This permitted the oral administration of 60 gr. (4 Gm.) of sulfapyridine in divided doses to be given daily for the next two days. It was then stopped because of the rapidly improving general condition. The blood sulfapyridine level was 5.1 mg. per 100 c.c. three days following hospitalization. An urticaria developed on the seventh day and remained until the eleventh day. A daughter furuncle occurred in the neck and was drained; with these exceptions the patient's convalescence was uneventful.

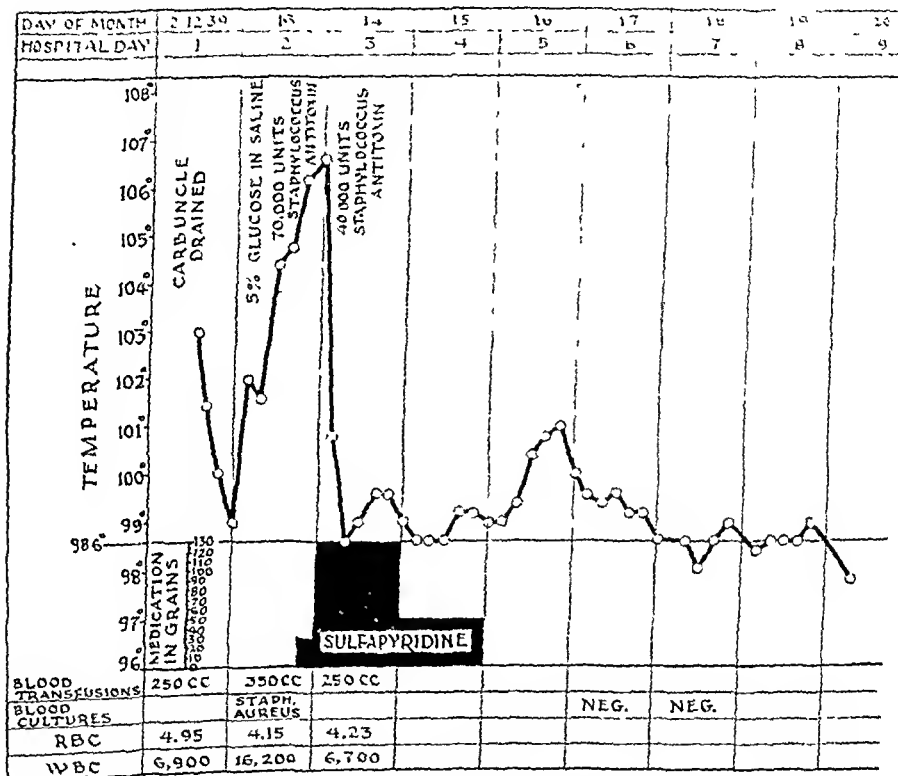


FIG. 3.—The effect of a combination of sulfapyridine and staphylococcus antitoxin on a child ten years of age with a *Staphylococcus aureus* septicemia

BACTERIOPHAGE

This form of therapy has been advocated for the treatment of a variety of bacterial infections. Staphylococcal infections are included in the group. There have been many cases of dermatitis, furunculosis, and septicemia treated with phage. In considering the efficiency of this form of therapy Longacre⁶⁰ says, "the evidence is equivocal and in many instances indicates that bacteriophage treatment in these lesions has no advantage over other forms of specific therapy." The potency of phage is important and some investigators think that this factor alone accounts for the disrepute into which phage therapy has fallen.

lococci that are susceptible to these drugs. Certain experimental observations indicate that none of these drugs, however, have any effect upon the toxins produced by some strains of staphylococci. Sulfanilamide, sulfapyridine, and sulfathiazole have little if any therapeutic value in the treatment of staphylococcal infections. The newer chemotherapeutic agents have been used for an insufficient period to satisfactorily evaluate them from a therapeutic standpoint.

It would seem that a combination of staphylococcal antitoxin and either sulfapyridine or sulfathiazole is the most satisfactory form of therapy, especially for those cases of severe staphylococcal infections in which the patient presents signs of a toxemia. This combination is most important if the staphylococcus is hemolytic. The antitoxin will neutralize any toxin that has not united with the tissue cells. As far as we know, neither antitoxin nor any chemotherapeutic agents will have any effect on the tissues injured by both the bacteria and the toxin previous to the administration of the drugs. The sulfanilamide derivatives may act directly or indirectly on the bacteria and thereby diminish the formation of toxin. The need for continuing the use of antitoxin will be determined by the individual case. The maximum effects from the antitoxin when used in combination with a chemotherapeutic agent will occur within the first few days of the disease.

Chemotherapy and serotherapy in staphylococcal infections cannot replace surgery. To drain a localized lesion is to eliminate a potential focus for the formation of toxin and the point from which bacteria may enter the circulating blood. Supportive measures are always indicated, such as transfusions for the anemia. The albumin-globulin ration in the blood should be retained, as should the sugar and the chloride levels. From the immunologic standpoint one must always remember that active immunity to staphylococcal infections develops slowly and the period of its efficiency is not known. On the other hand, passive immunity manifests its action immediately and its effect persists for only a few days.

CONCLUSION

One important way in which staphylococci may effect the host is through the effect of its toxin on the parenchymatous tissues. The exotoxin produced by the staphylococcus may be neutralized by specific antitoxin. It is necessary to give the antitoxin before the toxin becomes fixed to the tissues. Toxin apparently is present in over 90 per cent of the cases of staphylococcal septicemia. It is capable of producing death or it may be only of secondary importance in the pathologic processes.

The action of the chemotherapeutic agents apparently depends upon their inhibitory influence on bacterial growth. They do not neutralize staphylococcal toxin. It is difficult to accurately determine at this time their clinical efficiency.

of patients treated with toxoid and concludes at this time that "Staphylococcal toxoid injected intramuscularly is a safe antigen giving rise to a relatively small number of minor reactions. Staphylococcal toxoid gives a good clinical result in a high proportion of cases of recurrent and resistant furunculosis, and is useful in the treatment of styes and carbuncles. It is not effective in pustular acne and syecosis with the dose employed in this series."

DISCUSSION

It appears at the present time that any rational approach to the problem of therapy in staphylococcal infections is difficult. This no doubt results from the wide variation in the action of different strains of staphylococci and also in our inability to satisfactorily classify them as of the pathogenic and the nonpathogenic strains. The coagulase test may be the most satisfactory method at present for the separation of the pathogenic and nonpathogenic organisms; however, the division into hemolytic and nonhemolytic strains is very important. The rapidity in which the latter division can be made is valuable from a clinical standpoint. The hemolysis as observed on blood agar media in which rabbit red cells are used occurs earlier and forms a larger zone than with any other known type of blood agar medium.

Staphylococcus antitoxin that neutralizes the hemolytic factor in staphylococcus toxin also will neutralize the so-called skin necrotizing factor, the nephrotoxin, and the acute killing factors.

The role that staphylococcus toxin may play in certain staphylococcal infections has been discussed. Antitoxin apparently is the only therapeutic agent that will neutralize the toxin and thus eliminate its action upon the tissues. Antitoxin is indicated in those cases in which there are the clinical manifestations of a toxemia. It is of questionable value, however, in cases of localized staphylococcal infection such as chronic osteomyelitis and carbuncles. It is not indicated in cases of recurrent furunculosis. The antitoxin should be given early in the disease and in large quantities. The dose should be an amount sufficient to produce an excess of antitoxin in the circulating blood. The minimum dose should be 100,000 units preferably given intravenously. In severe infections with profound toxemia 300,000 to 400,000 units of antitoxin may be required. This foreign protein is rapidly eliminated from the body and is usually absent from the blood in five to seven days. Parrish's technique may be used to demonstrate antitoxin in the blood.²⁶ The appearance of natural or spontaneous antitoxin in the blood in the absence of irreparable damage to important viscera is in our opinion a favorable sign.

Certain of the sulfanilamide derivatives are bacteriostatic and in the presence of sulfanilamide an increase in phagocytosis in vitro has been observed. Information at this time is meager as to the strains of staphy-

26. Parrish, H. J.: Staphylococcal Toxin, Toxoid and Antitoxin, *Lancet* 1: 1054, 1934.
27. Carrol, G., Kappel, W., Jones, L., Gallager, F. W., and Di Rocco, P. W.: Sulfamethylthiazol; A Report of Its Clinical Use in Staphylococcus Septicemia With Apparent Success; Report of Animal Experiments, *South. M. J.* 33: 83, 1940.
28. Barlow, O. W., and Homburgh, W. E.: Specific Chemotherapy of Experimental Staphylococci Infections in Mice, *Proc. Soc. Exper. Biol. & Med.* 42: 792, 1939.
29. Bliss, E. A., and Ott, E.: Effect of Sulfapyridine, Sulfathiazole and Sulfamethylthiazole Upon Severe Staphylococcal Infections in Mice, *Proc. Soc. Exper. Biol. & Med.* 43: 706, 1940.
30. Bliss, E. A., and Long, P. H.: Comparative Therapeutic Effects of Sulfapyridine in Experimental Staphylococcus Aureus Infections in Mice, *Proc. Soc. Exper. Biol. & Med.* 40: 32, 1939.
31. Feinstone, W. H., Bliss, E. A., Ott, E., and Long, P. H.: Observations Concerning the Toxicity, Absorption and Therapeutic Effects of Sulfanilamide and Certain Related Organic Sulfur-Containing Compounds in Experimental Infections in Mice, *Bull. Johns Hopkins Hosp.* 62: 565, 1938.
32. Mellon, R. R., Shinn, L. E., and McBroom, J.: Therapy of Experimental Staphylococcus Infections With Sulfanilamide Compounds, *Proc. Soc. Exper. Biol. & Med.* 37: 563, 1937.
33. Rake, G., and McKee, C. M.: Action of Sulfathiazole and Sulfamethylthiazole on Staphylococcus Aureus, *Proc. Soc. Exper. Biol. & Med.* 43: 561, 1940.
34. Whitby, L. E. H.: Chemotherapy of Bacterial Infections, *Lancet* 2: 1095, 1938.
35. Browning, P.: The Chemotherapy of Experimental Staphylococcal Infection in Mice With Drugs of the Sulfanilamide Group, *J. Path. & Bact.* 50: 431, 1940.
36. McDonald, A.: Sulphamethylthiazole in Experimental Staphylococcal Infection, *Lancet* 1: 1157, 1940.
37. Kendrick, J. I.: Staphylococcus Septicemia With Septic Arthritis of Knee Treated With Sulfapyridine; Report of a Case, *Cleveland Clin. Quart.* 7: 35, 1940.
38. Blumenthal, J. S.: Sulfapyridine in the Treatment of Staphylococcus Septicemia, *Minnesota Med.* 23: 122, 1940.
39. Pegau, P. M., and Reed, C. C.: A Case of Staphylococcus Septicemia With Recovery by the Use of Sulfapyridine, *J. M. Soc. New Jersey* 37: 111, 1940.
40. Gill, A. M.: Staphylococcal Meningitis Treated With Sulfapyridine Recovery, *Brit. M. J.* 1: 810, 1940.
41. Morrison, L. F., and Schnider, M.: Cavernous Sinus Thrombosis; Report of Recovery Following Sulfapyridine Therapy, *Arch. Otolaryng.* 31: 948, 1940.
42. Martin, W. B., and Ginman, R. B.: The Treatment of Severe Staphylococcus Infections With Sulfapyridine and Its Sodium Salt, *South. M. J.* 33: 1039, 1940.
43. Farrell, L. N.: Appraisal of Therapeutic Agents in Experimental Staphylococcal Infection, *Brit. J. Exper. Path.* 21: 302, 1940.
44. Carpenter, C. M., Barbour, G. M., and Haeley, P. L.: The Inactivation of Staphylococcal Toxin in Vitro by Sulfanilamide, *J. Pediat.* 14: 116, 1939.
45. Carpenter, Charles M., and Barbour, Gerald M.: Inactivation of Toxins of Staphylococcus Aureus and Clostridium Welchii in Vitro by Sulfanilamide, *Proc. Soc. Exper. Biol. & Med.* 41: 354, 1939.
46. Rigdon, R. H., and Freeman, P. R.: Experimental Study of the Effects of Sulfapyridine on Staphylococci and Staphylococcus Toxin, *J. Lab. & Clin. Med.* 25: 1125, 1940.
47. Baylis, M.: Effect of Sulfanilamide, Sulfapyridine, and Sulfathiazole on Staphylococcus Toxin, *Proc. Soc. Exper. Biol. & Med.* 44: 525, 1940.
48. Lawrence, C. A., and Barker, O. W.: Bacteriostatic Actions of Three Thiazol Derivatives of Sulfanilamide Upon Bacteria in Both Cultures, *Proc. Soc. Exper. Biol. & Med.* 43: 92, 1940.
49. Editorial: Septicemia and Bacteremia, *Lancet* 2: 265, 1940.
50. Alys, Edwin P., and Roberts, Louis C.: Chemotherapy in Non-specific Infections of the Urinary Tract, *J. A. M. A.* 115: 1345, 1940.

A combination of chemotherapy and serotherapy may offer the best results in the treatment of staphylococcal septicemia. The efficiency of any form of treatment, of course, is in direct ratio to the duration of the infection, the toxin producing ability of the organism, and the resistance of the host. The earlier any treatment is begun the better will be the therapeutic response.

Chemotherapy and serotherapy are only adjuncts to surgery. They should not be considered as agents to replace it in the treatment of localized staphylococcal infections.

REFERENCES

1. Blair, John E.: The Pathogenic Staphylococci, *Bact. Rev.* 3: 97, 1939.
2. Chapman, George H., Berens, Conrad, Nilson, Edith L., and Curcio, Lillian G.: *J. Bact.* 35: 311, 1938.
3. Flaum, Alfred: Studies in Staphylococci and Staphylococcal Immunity, *Acta Path. et Micro. Scand.*, Suppl. 35, 1938.
4. Rigdon, R. H.: Staphylococcus Immunity; Resume of Experimental and Clinical Studies, *Arch. Path.* 24: 233, 1937.
5. Rigdon, R. H.: Staphylococcus Toxin, A Resume, *Am. J. M. Sc.* 199: 412, 1940.
6. Rigdon, R. H., and Harris, Henry: Deterioration of Staphylococcal Toxin in Saline, *Proc. Soc. Exper. Biol. & Med.* 39: 585, 1939.
7. Rigdon, R. H.: Effect of Heat on the Hemolytic and Skin Necrotizing Factors in Staphylococcus Toxin, *J. Lab. & Clin. Med.* 24: 142, 1938.
8. Gross, H.: Die Kulturfiltratstoffe der Staphylokokken und deren Beziehungen Zueinander, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* 73: 14, 1931.
9. Rigdon, R. H.: Hemolysis Produced by Staphylococcus Colonies and Toxin on Agar, *J. Lab. & Clin. Med.* 24: 1264, 1939.
10. De Christinas, M. J.: Recherches Experimentales sur la Suppuration, *An. Inst. Pasteur* 2: 469, 1888.
11. Rigdon, R. H., and Leff, W. S.: A Gastrointestinal Lesion Associated With Staphylococcus Infection in Man, *Arch. Path.* 21: 298, 1936.
12. Rigdon, R. H.: Renal Lesions in Staphylococcus Aureus Infection and Their Relation to Acute Glomerular Nephritis, *Arch. Int. Med.* 57: 117, 1936.
13. Rigdon, R. H.: Experimental Nephritis Produced by Staphylococcus Toxin in the Dogs, *J. Lab. & Clin. Med.* 24: 935, 1939.
14. Stookey, Paul F., Ferris, Carl R., Parker, Hubert M., Scarpellino, Louis A., and English, Kim E.: Necrotizing Ulcers Complicating Erysipelas, *J. A. M. A.* 103: 903, 1934.
15. Stookey, Paul F., and Scarpellino, Louis A.: Dermonecrotic Properties of Staphylococcus Filtrates, *South. M. J.* 28: 148, 1935.
16. Rigdon, R. H.: Local Lesions Produced in Mice by Staphylococcus Toxin and by Toxin and Non-Toxin Producing Strains, *SURGERY* 6: 91, 1939.
17. Farrell, L. N., and Kitching, J. S.: Passive Protection of Mice With Immune Horse Serum Against Living Staphylococci, *J. Path. & Bact.* 50: 439, 1940.
18. Burnett, F. M.: The Exotoxin of Staphylococcus Pyogenes Aureus, *J. Path. & Bact.* 32: 717, 1939.
19. Stookey, P., Scarpenella, L., and Weaver, James B.: Immunology of Osteomyelitis, *Arch. Surg.* 32: 494, 1936.
20. Joyner, A. L., and Smith, D. T.: Acute Staphylococcus Osteomyelitis, *Surg., Gynec. & Obst.* 63: 1, 1936.
21. Dolman, C. E.: Staphylococcus Antitoxic Serum in the Treatment of Acute Staphylococcal Infections and Toxemias, *Canad. M. A. J.* 30: 601, 1934.
22. Baker, Lenox D., and Shands, Alfred R.: Acute Osteomyelitis With Staphylococemia, *J. A. M. A.* 113: 2119, 1939.
23. Williams, S. W.: The Early Treatment of Acute Osteomyelitis, *M. J. Australia* 2: 459, 1937.
24. Stookey, Paul F., and Scarpellino, Louis A.: Staphylococcus Septicemia, *South. M. J.* 32: 173, 1939.
25. Council on Pharmacy & Chemistry: Staphylococcus Antitoxin, *J. A. M. A.* 116: 684, 1940.

Editorial

The Delayed Classification of Burns

CERTAIN techniques of medical thought, originally contributions of value, may, although they have outlived their usefulness, become so ingrained in the literature that they remain to becloud rather than illuminate the subject. In this class may be placed, perhaps, the commonly accepted American classification of burns into three "degrees."

Within obvious limits, the surface area governs the mortality of a burn and the depth, the morbidity. The purpose of measurement of extent is to afford prognostic data as to survival; the purpose of measurement of depth, that is, "degree," is to afford prognostic data as to the time of healing and the necessity for skin grafting. The only useful classification of depth would be one to give that information.

"First degree" and "second degree" burns, of course, present no problem of depth. There is no marked loss of tissue and, hence, little epithelial growth is initiated. Even the severest of them needs only the replacement of incompletely destroyed surface epithelium. If infection is excluded and the burned area is not large enough to cause death, such burns are always well within a few days.

If we examine, however, the severest degree permitted by the traditional classification we find a different state of affairs. By definition, a "third degree" burn means a burn that is deep enough to entail loss of substance, but it does not define the depth of loss. And in that deficiency resides its lack of usefulness as a description of prognostic significance.

To appreciate the truth of this statement, one need only consider the processes of healing at various depths of burning. If destruction includes the entire dermis, then epithelization must proceed from the edges only; if it includes only a part of the skin depth, then healing will occur throughout the burned area from thousands of minute epithelial elements, the remaining fragments of papillae, hair follicles, and glands. In the former instance spontaneous healing accompanied by scar contracture is a matter of months, if it ever occurs, and even a relatively satisfactory result depends upon skin grafting. In the latter instance, however, if infection and chemical abuse are avoided, one cannot prevent healing, a process usually complete within three weeks and accompanied by no contracture of scar. And yet these two diverse pictures are included under a single classification.

The reason for the tenacity of a poor term is not too hard to understand. The depth of a burn in relation to full or partial thickness of

51. Helmholtz, H. F., and Larson, Nora: The Use of Sulfathiazole as a Urinary Antiseptic, *Proc. Staff. Meet., Mayo Clin.* 15: 651, 1940.
52. Dietel, Frederick W., and Kaiser, Albert D.: *Staphylococcus Aureus Meningitis Successfully Treated With Sulfathiazole*, *J. A. M. A.* 115: 601, 1940.
53. Fitch, Thomas S. P.: Sulfathiazole in *Staphylococcus Aureus*, *Arch. Pediat.* 57: 119, 1940.
54. Spink, Wesley W., and Paine, John R.: The Local Use of Sulfathiazole in the Treatment of Staphylococcal Infections, *Minnesota Med.* 23: 615, 1940.
55. Long, Perriu H., and Haviland, James W.: The Problem of Pneumonia With Reference to Chemo- and Sero-Therapy, *Ann. Int. Med.* 14: 1042, 1940.
56. De, S. P., and Basu, U. P.: Synergy in Experimental Chemotherapy of Staphylococcal Infections, *Brit. M. J.* 2: 564, 1938.
57. Editorial: Generalized Staphylococcal Infection, *Lancet* 2: 1076, 1939.
58. Farrell, Leone N.: Combined Action of Sulfapyridine and Serum in Experimental Infection in Mice, *Canad. Pub. Health J.* 31: 27, 1940.
59. Goldberg, Samuel L., and Bloomenthal, Ernest D.: Staphylococci Septicemia, *SURGERY* 9: 508, 1941.
60. Longacre, Alfred B.: Immunologic Prophylaxis and Therapy in Human Staphylococcal Infections, *South. Surgeon* 10: 247, 1941.
61. Larkum, N. W.: Relationship of Bacteriophage to Toxin and Antitoxin, *Proc. Soc. Exper. Biol. & Med.* 30: 1395, 1930.
62. Dutton, L. O.: Therapeutic Use of Bacteriophage With Special Reference to *Staphylococcus*, *Southwestern Med.* 17: 374, 1933.
63. Jern, Helen, and Meleney, Frank L.: Studies in Bacteriophage, *J. Lab. & Clin. Med.* 22: 284, 1936.
64. McNeal, W. J., and Frisbee, F. C.: Bacteriophage as a Therapeutic Agent in *Staphylococcus Septicemia* Receiving Bacteriophage Service, *Am. J. M. Sc.* 191: 179, 1936.
65. Dolman, C. E.: Treatment of Localized Staphylococci Infections With Staphylococcus Toxoid, *J. A. M. A.* 100: 1007, 1933.
66. Pantan, P. N., and Valentine, F. C. O.: Staphylococcal Infection and Re-infection, *Brit. J. Exper. Path.* 10: 259, 1929.
67. Murray, D. S.: Staphylococcus Toxoid, Clinical Trial, *Lancet* 1: 303, 1935.
68. Barber, H. W., and Forman, L.: The Results of Intradermal Tests in Certain Dermatoses and the Therapeutic Effect of Intradermal Vaccines, *Brit. J. Dermat.* 45: 4, 1932.
69. Nelis, P.: L'immunité Antitoxique Staphylococcique, *Rev. d'immunol.* 1: 152, 1935.
70. Klotz, D., and Holman, W. L.: Studies on Staphylococci, *Am. J. M. Sc.* 189: 436, 1935.
71. Burnet, F. M.: The Exotoxins of *Staphylococcus Pyogenes Aureus*, *J. Path. & Bact.* 32: 717, 1929.
72. Conner, J. I., and McKie, M.: Treatment of Superficial Staphylococcal Infection by Toxoid, *Brit. J. Dermat.* 46: 20, 1934.
73. Nelis, P.: Une Nouvelle Thérapeutique des Staphylococcies la Vaccinothérapie par l'Exotoxine, *Presse méd.* 43: 1141, 1935.
74. Dolman, C. E.: The Use of Staphylococcus Toxoid, *Lancet* 1: 306, 1935.
75. P. Ritossa, and ...: Staphylococci Toxoid in Staphylococcal Infection, *J. A. M. A.* 114: 1025, 1940 (abstract).
76. Council on Pharmacy and Chemistry: Staphylococcus Toxoid, *J. A. M. A.* 104: 562, 1935.
77. Whitby, L. E. H.: Modern Treatment of Staphylococcal and Pneumococcal Infections, *Lancet* 2: 779, 1934.
78. Whitby, L. E. H.: The Treatment of Staphylococcal Skin Lesions With Toxoid *Lancet* 1: 1454, 1936.

the general acceptance of Dupuytren's classification would adequately fulfill the purpose of the present proposal.

The observers who are studying burns during the present acute interest in them, are, of course, well aware of the importance of the critical level between Groups II and III. The majority of readers of the ever-growing literature may not be thinking in these terms. To them all "third degree" burns may be the same and may offer the same problems and the same prognosis; this fogginess of thought will continue as long as the authorities continue to present two distinct conditions under one heading. It may be that the present lack of unanimity of opinion on the proper local therapy for burned surfaces has arisen because of the failure to discriminate between degrees within the "third degree." Certainly the literature is full of photographs of so-called response to specific types of therapy in individual burns that would obviously heal promptly under any nondestructive regime. A recent striking moving picture of a theoretically sound method of therapy shows just such a burn. The less experienced might believe that all "third degree" burns will heal in a manner equally dramatic and prompt.

If a more rational classification yields dependable evidence in guiding local therapy, the gain will outweigh the disadvantage entailed by delayed classification in the individual case. There is no point in attempting to measure the depth of a burn before it is possible to do so.

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the skin cannot be judged on inspection when first seen. The history may allow a guess as to probabilities. The high-temperature, short-duration burn (for example, from a gasoline explosion without ignition of the clothing) is more apt to be superficial than the low-temperature, long-duration burn (for example, the scald from more than momentary immersion in water close to 100° C.), yet on superficial inspection the appearances of the two may not differ. Even were a biopsy permissible, it might not yield the desired information since the deep limits of many burns cross and recross the critical level, leaving islands of preserved gland epithelium scattered throughout an expanse of complete thickness destruction. In other words, the diagnosis of the one thing important in prognosis as to morbidity is impossible at the time many burns are first seen. Only examination after sloughing has occurred will furnish the desired information. What is needed in classifying burns is the general recognition of this fact.

A classification may be suggested in which this limitation is accepted. A simplification of Dupuytren's classification is proposed, dividing all burns into three groups, which will be separately defined and discussed below. In order to make a sharp departure from traditional thought, the use of the word "group" is suggested rather than "degree." The classification is based almost entirely upon the therapeutic problems involved.

The proposed classification is as follows:

Group I. This is the most superficial type of burn and includes all burns now classified as "first and second degree." The reason for combining the two under one head is that there is little difference in treatment and none in prognosis. In many instances the diagnosis of a Group I burn can be made on first inspection.

Group II. All burns involving loss of substance in which the loss nowhere includes the full thickness of the skin. This group requires protection from damage and contamination, takes somewhat longer to heal than Group I, but does not require skin grafting for a satisfactory result. It cannot be diagnosed until after sloughing has occurred.

Group III. This burn includes the full thickness of the skin and any structures beneath. It requires skin grafting for a satisfactory result. It also cannot be diagnosed until removal of the slough. Many, if not most, of Group III burns will present peripheral or central areas of Group I and Group II destruction. This latter fact is of no practical significance since these areas will declare themselves before skin grafting can be undertaken.

Group III corresponds to the fourth and higher degrees of Dupuytren's classification. It is interesting that the value of Dupuytren's grouping has not been recognized in American thought. Perhaps impatience to offer an immediate prognosis is the explanation. Certainly

out that while such lesions occur also in various conditions other than hyperthyroidism, they were encountered so consistently in their series of autopsies (in all but 9 of the 107 cases, or 91 per cent) that it was felt impossible to ignore them as a characteristic feature of the disease. In five of their cases the lesions were so pronounced as to be comparable to those found in moderately severe acute yellow atrophy. Raab and Terplan⁵⁹ and Kerr and Rusk⁴⁰ also reported finding degenerative liver lesions in hyperthyroidism similar to those found in acute yellow atrophy.

Two types of chronic lesions, also, were described by Beaver and Pemberton. The first and most important of these was a condition which they designated "chronic atrophy," the term referring to the loss of weight of the liver.* This change was found in 66.55 per cent of the livers examined. It was frequently associated with the acute degenerative changes described above, and at times with some degree of cirrhosis. In many instances when the acute degenerative lesions were not present, no histologic change was found in these atrophic livers. In some instances, however, the liver cells were small and at times there was some increase in the connective tissue, which in certain cases was limited to the hepatic tissue near Glisson's capsule.

The second chronic lesion described by these authors was cirrhosis, present in about 60 per cent of their series, and apparently a late stage of the acute and atrophic changes described above. The microscopic changes found in association with the cirrhosis they considered similar to the "chronic parenchymatous interlobular hepatitis" described by Weller.⁶⁰

Weller, in 1933, studied forty-eight autopsies performed on patients dying with exophthalmic goiter and contrasted the liver lesions with those found in an equal number of carefully selected autopsies on patients dying from other causes. This author found various degenerative lesions in the livers of patients dying of Graves' disease, such as cloudy swelling, fatty infiltration, and pigment atrophy. These he considered might be due to the direct effect of thyrotoxicosis; but he pointed out, as did Beaver and Pemberton,⁹ that this cannot be proved, since such lesions are frequently encountered also in autopsies on patients dying from other causes. One type of lesion, however, he considered specifically associated with Graves' disease, and described as a "patchy, chronic, parenchymatous, interlobular hepatitis," involving the peripheral portion of the lobules to a moderate degree and showing more fibrosis and lymphatic infiltration than bile duct proliferation. He found chronic hepatitis in forty-two of the forty-eight autopsies on patients dying with Graves' disease, while in the control series it was found in but fifteen instances, being well marked in only one.

*It is interesting that hyperthyroidism in animals produces hypertrophy of the liver; possibly the end stage of this would be atrophy.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

LIVER CHANGES IN HYPERTHYROIDISM

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INTRODUCTION

IN VIEW of the intense and varied metabolic activity of the liver, it would seem reasonable to assume that this organ especially would feel the increased drive of hyperthyroidism and in the recent literature increasing emphasis has been placed on the clinical importance of the liver changes occurring during this disease. Evidence of these changes is given by jaundice,^{9, 46, 65} which not infrequently occurs in association with the more severe forms of thyrotoxicosis, by other disturbances of liver function measurable by various laboratory tests,^{7, 46, 49, 61, 70} and by liver lesions often found at autopsy in those dying of the disease.^{9, 12, 65, 60} Whether the injury is due to the effect of increased amounts of the thyroid hormone on the liver cells, or to the injurious action of some other substance or factor on a liver made vulnerable by the functional strain of hyperthyroidism, is a moot point.⁵¹ The weight of evidence in the opinion of the reviewer seems to favor the latter theory. In any case, damage to the liver must be taken into consideration in the clinical management of a case of hyperthyroidism, particularly when the added stress of anesthesia and operation must be faced. It would seem, therefore, that an evaluation of the problem and a consideration of the possible available therapeutic measures to minimize or prevent the hazard of liver injury associated with hyperthyroidism might prove useful.

POST-MORTEM DATA

Liver lesions in wide variety have been found at autopsy in patients dying of hyperthyroidism, and have been reported in the literature by various authors.

Beaver and Pemberton⁹ in their analysis of 107 autopsies on patients dying with exophthalmic goiter noted two outstanding types of hepatic change, acute and chronic. The acute changes they described as fatty metamorphosis and central or focal necrosis. These authors pointed

tral necrosis of the liver lobules that he observed at times. Fatty changes occurred so frequently and were of such severity that this author felt they must be taken into account, although he pointed out, as have others before him, that they occur also in many conditions other than hyperthyroidism. In regard to cirrhosis, he found this lesion in 25 per cent of his autopsies on patients dying of hyperthyroidism, while in a control series the incidence was only 4.7 per cent. Shaffer further noted that the occurrence of cirrhosis did not appear to depend on deficiencies of vitamins A and C.

Lord and Andrus⁴⁵ carried out various studies on 680 patients with hyperthyroidism who had been subjected to some type of operation on the thyroid gland during the previous eight years. Sixteen of these patients had died, eight of them in typical thyroid crisis. Six of the sixteen were autopsied and the pathologic changes found in the liver were said to resemble those described by Beaver and Pemberton.⁹

In summary, numerous studies have been carried out on autopsy material from patients dying of hyperthyroidism, and the frequent occurrence of liver changes, both acute and chronic, has been reported. The acute lesions varied from minor fatty changes to degeneration so severe that it was comparable to that found in acute yellow atrophy. The chronic changes consisted of hepatitis, cirrhosis, and atrophy, and at times both acute and chronic lesions were found in the same liver.

Two series of autopsy studies on hyperthyroid patients have been reported by Means,⁵⁴ and Lewis,⁴⁵ who did not find the liver lesions impressive. Means, in commenting on the liver changes reported by other authors, as described above, considered that these lesions were probably a complication of thyrotoxicosis rather than an integral part of the disease. He believes it likely that the liver under conditions of hyperthyroidism is particularly vulnerable to various types of injury, possibly due to its depletion of liver glycogen or to other causes.

CLINICAL EVIDENCE

Jaundice.—In addition to post-mortem data pointing to liver damage in association with hyperthyroidism, we have clinical evidence in jaundice, which occurs as an occasional complication of this disease.

Case reports of jaundice occurring in hyperthyroidism have for a long time appeared in the literature at infrequent intervals. In 1874, Habershon³⁰ reported such a case in which the jaundiced patient was a young woman, 20 years of age, suffering from exophthalmic goiter complicated by rheumatic fever. At autopsy the pericardium was found to be acutely inflamed and covered with "shaggy membrane"; but there was no apparent liver lesion. Sutcliffe and Durh,⁶⁸ in 1898, reported "an extraordinarily acute case of Graves' disease" in which slight jaundice developed. The patient died three months after the first symptoms; there was no autopsy. In 1906, Eder²¹ reported three

Cirrhosis of the liver in association with exophthalmic goiter has also been reported by Marine and Lenhart,⁵⁰ who state that this condition has been observed in a significant number of long-standing cases coming to autopsy. These authors noted that the connective tissue increase varied from a slight thickening of the portal spaces to well-marked, fibrous bands, while the liver cells themselves usually showed some fatty changes. Goodpasture,²⁶ in reporting autopsies on two patients dying of exophthalmic goiter, stated that the liver in one case was definitely cirrhotic and in the other showed central congestion, moderate fatty changes, and numerous vacuolated nuclei. Widespread pathologic changes consisting of congestion, fatty infiltration and degeneration, necrosis, inflammation, and connective tissue proliferation were noted by Habán²⁹ in the livers of patients dying of exophthalmic goiter. He considered that these lesions were caused by the toxic action of the disease and to denote their specific nature he proposed the term "cirrhosis basedowiana," or "hepar basedowanum."

Cameron and Karunaratne,¹² in a study based on autopsies of 40 cases of proved exophthalmic goiter, classified the liver changes in 4 groups: first, passive venous congestion, of which there were 10 cases; second, fatty changes with or without necrosis, of which there were 5 cases; third, atrophy and nodular formation, likewise 5 cases; and, fourth, cirrhosis, 10 cases. In summary, they found that 2 out of 3 cases showed liver changes independent of passive venous congestion and they considered it possible to distinguish between cases in which passive venous congestion resulting from cardiac failure was primarily responsible for the pathologic changes and those in which the changes occurred independently of stasis, agreeing in this with Habán. Fatty changes occurred frequently and they attached little significance to this finding unless associated with definite necrosis, in which event they regarded the condition as evidence of toxemia and probably the basis for the chronic findings that they described as atrophy and cirrhosis.

Boyce and McFetridge,¹⁰ found liver changes at autopsy in six cases where the patient had died in a thyroid crisis. The lesions were classified as "fatty infiltration or degenerative changes ranging from mild changes to actual necrosis, cirrhotic changes, and acute yellow atrophy." The authors further stated that, "frequently the same liver revealed various degrees of all changes in different areas and as a rule there was a significant decrease in weight."

Another series of autopsies upon patients dying with hyperthyroidism was analyzed by Shaffer⁵⁵ from the Cincinnati General Hospital. This author found a high incidence of hepatic lesions, more than one type of lesion being present in the majority of the livers examined. The change that he considered of greatest significance was a chronic interstitial hepatitis, sometimes associated with cirrhosis. These lesions were not considered to be the result of chronic passive congestion, as was the cen-

Rosenthal modification of the phenoltetrachlorophthalein test, found that twenty-two of their forty-four hyperthyroid patients showed evidence of liver injury. The bromsulfalein test, used by Maddock and associates,⁴⁹ indicated impaired liver function in eight of thirteen patients (or 61 per cent).

Glucose, galactose, and levulose tolerance tests have also been used to provide an indication of liver function in the presence of hyperthyroidism. Youmans and Warfield,⁵⁰ working with glucose, found that nearly all their cases showed some abnormality in the characteristic curve of the blood sugar concentration, but were unable to correlate these abnormalities with the indications of liver damage afforded by the phenoltetrachlorophthalein test. Althausen and Wever⁴ reported that the curve of galactose in the blood after oral administration was considerably elevated in patients with hyperthyroidism. They believed this might be accounted for by impaired utilization of galactose by the liver, or possibly by accelerated intestinal absorption. Lichtman⁴⁶ also carried out galactose tolerance tests on thirteen patients with hyperthyroidism, in seven of whom he found a normal galactose excretion, while in six pathologic galactosurias were encountered. This author further noted a definite tendency for galactose tolerance to improve during the course of iodine therapy. Levulose tolerance tests were used by Youmans and Warfield,⁵⁰ who concluded that this method was definitely inferior to the phenoltetrachlorophthalein test in detecting impaired liver function.

It is questionable how much significance should be attached to any of the various sugar tolerance tests as pointing to specific injury to the liver in hyperthyroidism, for it must be borne in mind that complex disturbances of carbohydrate metabolism are present in this condition, and also that the rate of sugar absorption from the alimentary tract is probably increased.⁴

Approaching the study of liver function during hyperthyroidism from another point of view, Maddock and co-workers⁴⁹ studied the blood amino acid nitrogen in these patients. No abnormal values were found; but this is not surprising, since the deaminizing function of the liver is lost only in the presence of extensive liver damage, such, for example, as occurs in the terminal stages of acute yellow atrophy.*

Cinchophen oxidation in cases of uncomplicated hyperthyroidism was studied by Lichtman⁴⁷ who found that disturbances of this process existed in sixteen of his twenty cases (or 80 per cent), indicating moderate impairment of liver function. Severe damage to the liver, however, was in no instance indicated.

*It should be noted that liver damage as severe as that found in acute yellow atrophy has been reported occasionally in patients with marked hyperthyroidism (Kerr and Rusk.)⁴⁰ Presumably, in these patients the blood amino acid nitrogen would show abnormal values.

cases of jaundice occurring in patients with exophthalmic goiter. All three patients recovered from the jaundice; one passed gallstones.

The causes of jaundice are obviously numerous; and some of the early case reports are open to criticism both because the jaundice may have occurred from some pathologic process entirely unrelated to the thyroid and also because the diagnosis of hyperthyroidism may have been inaccurate. With the added evidence, however, of later reports of the clinical and pathologic data in a relatively large number of cases of hyperthyroidism, it has become evident that while jaundice is not common in this condition it is by no means rare in the more severe cases. In 1919, Kohn⁴¹ analyzed a series of 56 cases of exophthalmic goiter and reported the occurrence of jaundice in five. Heilmeyer,³⁵ in 1931, reported that among 101 cases of exophthalmic goiter, 6 patients showed jaundice that could not be explained on any other basis. Weller,⁶⁰ in 1933, reported jaundice in 8 of 35 patients whose cases he analyzed. Beaver and Pemberton,⁹ also in 1933, reported the occurrence of this complication in 23 (21.5 per cent) of their series of 107 cases of exophthalmic goiter, pointing out, however, that the jaundice was slight in 17 instances and pronounced in only 6. In Shaffer's⁶⁵ group of 24 thyrotoxic patients,* studied in 1940, jaundice was present in 5 and well marked in 3. Lichtman,⁴⁸ in 1941, reported that among 26 cases of Graves' disease autopsied at Mount Sinai, jaundice occurred twice. Kerr and Rusk⁴⁰ reported the clinical and pathologic findings in a patient operated upon for hyperthyroidism from which he had suffered for about 3 months. He ran a rather stormy post-operative course during which he developed jaundice which gradually became deeper, death occurring 15 days after operation. On autopsy the liver showed almost complete loss of architecture with necrosis and cellular infiltration.

Liver Function Tests.—Various laboratory tests have been used to elicit further information as to possible alterations of liver function during hyperthyroidism.

Blood bilirubin in the presence of hyperthyroidism has been measured in the belief that increased amounts of this pigment in the blood stream, in the absence of excessive hemolysis of red cells or of obstruction of the excretory ducts, would indicate impaired function of the liver parenchyma. Youmans and Warfield⁷⁰ carried out this test in twelve cases and found increased bilirubin in seven. Maddock and collaborators⁴⁹ also reported finding hyperbilirubinemia in certain of their hyperthyroid patients.

Various dyes have been used to determine the functional efficiency of the liver in hyperthyroidism. Youmans and Warfield,⁷⁰ using the

*Three of the 24 patients were admitted in thyroid crisis and of these, 2 were jaundiced.

form of hyperthyroidism, it is not surprising that the various manifestations of depressed liver function, including jaundice and degenerative liver changes in those coming to autopsy, have frequently been found in such cases.^{10, 17, 49} Indeed, the theory has been advanced that the changes taking place in the liver are themselves responsible for the occurrence of the thyroid crisis,¹⁰ and a similarity has been seen between certain clinical features of the crisis, especially hyperpyrexia, and the syndrome that accompanies the so-called "liver deaths."^{10, 11, 44} Exception to this view is taken by Maddock and his co-workers,⁴⁹ who could find no correlation between the preoperative determination of hepatic function and the mildness or severity of the reactions following operations on the thyroid gland. These authors further point out that while an increase in the symptoms of hyperthyroidism together with a measurable decrease in liver function often occur postoperatively, they found nothing to show that one was the cause of the other. While to me also, the evidence seems weak in favor of the theory that the primary pathology responsible for the crisis is to be found in the liver, injury to the liver does undoubtedly occur frequently as a complication of the crisis, often playing an important part in the clinical picture and even contributing to a fatal outcome.

DATA FROM ANIMAL EXPERIMENTS

There is little exact information on the interrelationship of the liver and the thyroid under normal conditions. A survey of the literature, however, brings out several points. Complex iodine products in general are eliminated by the liver, and it is believed that this also applies to the thyroid hormone, its destruction and excretion taking place by means of this organ.^{1, 60} There is also some evidence that under certain conditions thyroxin may be stored in the liver.^{2, 3, 71} Thus, Zavodovsky and Azimov⁷¹ reported that after a large dose of thyroxin they were unable to find the hormone in the blood until after the lapse of four hours and they considered that during this interval the hormone was accumulating in the liver.

That certain changes are produced in the liver by experimental hyperthyroidism has been known for a long time.

Hypertrophy of the Liver.—As early as 1916, Hoskins³⁸ reported that in thyroid-fed albino rats the liver appeared considerably heavier than in the controls. In 1920, Hewitt³⁶ likewise reported a hypertrophy of the liver in thyroid-fed animals. In 1930, Simonds and Brandes⁶⁶ carried out an extensive study on dogs, in which body weights and liver weights were compared in normal, thyrotoxic, and starved animals. These authors found that whereas in starvation the liver lost weight in greater proportion than the body, in thyrotoxicosis the liver loss was less, proportionately, than that of the body as a whole. They point out that this is particularly striking since we know that glycogen is lost from

Recently, several investigations of liver function in hyperthyroidism have been carried out by using the Quick hippuric acid test, which is based on the assumption that the liver is involved in the conjugation of benzoic acid and glycine to form hippuric acid. Bartels⁷ found that reduction in liver function was shown by this test to exist in a high proportion of hyperthyroid patients, only 18 out of the 148 such patients giving a normal response at the time of admission to the hospital. The degree of impairment of liver function appeared to be in direct proportion to the severity of the hyperthyroidism. In cases of primary hyperthyroidism, improvement occurred during preoperative treatment; no change, however, was apparent in cases of adenomatous goiter with hyperthyroidism. Boyce and McFetridge¹⁰ and Haines and associates³² have also reported finding disturbances of liver function in hyperthyroid patients by use of the hippuric acid test. Haines and his co-workers go on to say, however, that since the reduction of hippuric acid excretion is not uniformly found in patients who are considered by other standards to be poor surgical risks, they do not consider this test to be of great value in the clinical management of patients with hyperthyroidism.

A different method of testing liver function was used in 1941 by Lord and Andrus.⁴⁸ These authors had previously found that patients with intrahepatic jaundice had reduced values of plasma prothrombin, and that on injection of 2-methyl-1, 4-naphthoquinone, the plasma prothrombin content did not rise significantly. In cases of extrahepatic jaundice, on the other hand, the plasma prothrombin did rise significantly following injection of this drug. These authors, therefore, suggested that the response of a low level of plasma prothrombin to the injection of 2-methyl-1, 4-naphthoquinone might be considered a measure of hepatic function. With this in mind they studied the level of plasma prothrombin in a series of thirty-six hyperthyroid patients and found that whereas the preoperative level of plasma prothrombin showed no direct correlation with the severity of the hyperthyroidism, a significant fall took place postoperatively in twenty-nine out of the thirty-six cases of toxic goiter and furthermore, that the extent of the fall could be closely correlated with the severity of the postoperative course. Apparently, however, these authors did not test the response of the patients to the injections of the 2-methyl-1, 4-naphthoquinone.

EFFECT OF THYROID CRISIS ON THE LIVER

Although the frequency of the thyroid crisis and postoperative storm has been greatly reduced by the introduction of iodine therapy, these reactions have by no means disappeared⁶ and probably account for over half the number of deaths resulting from thyrotoxicosis.^{6, 27, 49} Since patients developing these reactions suffer from the most severe

*Pemberton²⁸ points out that some reaction occurs after every operation for active exophthalmic goiter, although the typical severe reaction is no longer common.

and in those sacrificed at an earlier stage in the experiments. The lesions varied from relatively simple fatty degeneration to actual necrosis. They were most marked around the central veins, but at times involved the entire lobule. In the periphery of the lobules showing degenerative changes, he frequently found evidence of reparative processes, as indicated by a large number of mitotic nuclei and young cells with clear protoplasm and large nuclei. In animals dying after a long course of thyroid administration, there was evidence of chronic passive congestion.

In 1933, Gerlei,²⁴ working with rabbits, studied the effect produced on the liver by administering large amounts of thyroxin. The animals were given daily subcutaneous injections of 4 mg. of thyroxin and death ensued in four to five days. In addition to finding hypertrophy of all the organs, he found extensive degeneration and necrosis of the liver resembling that found in chloroform poisoning. The necrosis was most marked around the central veins, and while the necrotic areas themselves showed very little fat, the boundary zone between the necrotic and normal cells showed large amounts.

Liver Function Tests.—There are very few reports on liver function tests during experimental hyperthyroidism in animals. Younians and Warfield¹⁰ reported some preliminary experiments in which liver function was determined by use of the phenoltetrachlorophthalein test. These workers found that thyroid-feeding of their animals had no effect on the functional efficiency of the liver as estimated by the above test. Drill and Hays²⁰ studied the liver function in hyperthyroid dogs by means of the bromsulfalein method. They found that after prolonged feedings of thyroid extract to these animals, disturbance of liver function usually developed and the dye retention was greatly increased by reducing the amount of yeast in the diet or omitting it entirely. These authors do not claim that deficiencies of the B vitamins were the only factors in diminished liver function in their hyperthyroid animals, but they feel that there was some causal relationship between disturbances of liver function and the insufficient intake of these vitamins.

INCREASED SUSCEPTIBILITY OF THE LIVER TO INJURY UNDER CONDITIONS OF HYPERTHYROIDISM

Increased Susceptibility to Chloroform.—It has already been suggested that the liver under conditions of hyperthyroidism may be more susceptible to injury by various agents than it is normally. In order to test this hypothesis, a number of attempts have been made to ascertain the effect of various well-known liver poisons during hyperthyroidism. One of the first of such experiments was carried out by Davis and Whipple,¹⁶ who tried the effect of feeding thyroid to the experimental animals prior to the administration of chloroform by inhalation.

the liver in both starvation and hyperthyroidism, and that, consequently, something must occur in this organ to counterbalance the loss of liver weight which one would expect from the loss of liver glycogen in the thyrotoxic animals. These authors are inclined to the view that the relative, if not absolute, hypertrophy of the liver during experimental hyperthyroidism is caused by the increased and augmented blood flow to this organ.*

In 1933, Higgins³⁷ confirmed the finding that feeding thyroid extract to rats tended to produce an increase in the size of the liver. He further showed that when a subtotal removal of the liver was carried out, the rats receiving thyroid regenerated their liver tissue more rapidly than animals similarly operated upon but receiving no thyroid.

Change in Liver Glycogen.—Perhaps the most widely recognized effect produced in the liver by the increased thyroid hormone in the blood is a marked decrease in liver glycogen.† This important finding was first reported in 1913, by Cramer and Krause,¹⁵ and has since been confirmed by many other workers. Cramer and Krause carried out their work on cats and rats and reported that after small amounts of fresh thyroid gland had been administered for two or three days to these animals, even though they were on a carbohydrate-rich diet, the liver was found to contain only a trace of glycogen. They believed that this was due to an inhibition of the glycogenic function of the liver and not to an increased utilization of carbohydrates.

The above findings of Cramer and Krause were confirmed in 1917 and 1918, by Kuriyama,^{42, 43} and in 1933, by Coggeshall and Greene,¹³ who further reported that when thyroxin and desiccated thyroid gland were given in equi-iodine doses, the former preparation lowered the liver glycogen more than did the latter.

Drill¹⁹ reported in 1937, that he was able to maintain a normal level of liver glycogen in thyroid-fed rats by administering large doses of the vitamin B complex.

Histologic Changes.—Histologic changes are said to occur in the liver when experimental hyperthyroidism is produced in animals. One of the earliest studies on this aspect was carried out in 1913, by Farrant,²² who produced hyperthyroidism in cats and rabbits by feeding thyroid extract, and reported finding histologic changes in the liver, occurring most markedly in the center of the lobules. He described these changes as fatty degeneration.

In 1921, Hashimoto³⁴ produced hyperthyroidism in albino rats by feeding desiccated thyroid gland. This author was chiefly interested in the changes in the heart, but also reported finding pathologic changes in the liver both in animals dying during the course of the experiment

*The kidney and heart also show an increase in size.
†The phenomenon of decreased liver glycogen in hyperthyroidism is so constant that it has been suggested as a test for the presence of the thyroid hormone in unknown preparations (Dresel and Goldner)."

and in those sacrificed at an earlier stage in the experiments. The lesions varied from relatively simple fatty degeneration to actual necrosis. They were most marked around the central veins, but at times involved the entire lobule. In the periphery of the lobules showing degenerative changes, he frequently found evidence of reparative processes, as indicated by a large number of mitotic nuclei and young cells with clear protoplasm and large nuclei. In animals dying after a long course of thyroid administration, there was evidence of chronic passive congestion.

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These authors concluded that the administration of thyroid had no influence on the liver injury following chloroform anesthesia,* and that the only notable finding in the liver at autopsy was the unusually small amount of fat. These experiments are open to certain criticisms, in that only four animals (dogs) were used, that they received thyroid treatment for only four days, and that the chloroform was given by inhalation only and not by injection. The significance of this latter point is brought out by Goodpasture,²⁵ who, in studying the effects of light chloroform anesthesia on the myocardium of hyperthyroid animals, noted that although the thyrotoxicosis did increase the susceptibility of the heart muscle to the toxic action of chloroform anesthesia, the livers of these animals usually showed no central necrosis. When, however, the chloroform (in small doses of 0.2 c.c. per kg.) was administered subcutaneously, the animals usually died within twenty-four hours with extensive liver necrosis. No control experiments were carried out to show the effect of chloroform injections on the livers of animals not receiving thyroxin.

McIver,⁵¹ however, in 1940, showed that the administration of crystalline thyroxin to albino rats definitely increased their susceptibility to chloroform poisoning. The chloroform in these experiments was administered by subcutaneous injection, 0.4 to 1.5 c.c. per kg. of body weight, to animals that had received injections of crystalline thyroxin over a period of one to two weeks. Of fifteen animals (rats) so treated, eleven died in twelve to thirty-six hours, while four recovered. In the control group of twenty rats which received the chloroform injections but no preliminary treatment with thyroxin, all recovered or were sacrificed at the end of forty-eight hours, showing no symptoms of chloroform poisoning. In 1942, McIver and Winter,⁵² in experiments on the mechanism of the increased susceptibility to chloroform poisoning found in hyperthyroid rats, showed that it could not be attributed simply to the fact that the liver glycogen is depleted by the administration of thyroxin. These authors further showed that the administration of a high protein diet did not protect the livers of the hyperthyroid rats from injury following chloroform injections.

Carbon Tetrachloride Experiments.—Cameron and Karunaratne,¹² in 1935, could not find that liver damage from toxic doses of carbon tetrachloride was increased by feeding thyroid extract to the rats.

Effects of Intercurrent Infection.—There is some evidence in the literature that the liver of hyperthyroid animals is particularly susceptible to intercurrent infection. Thus, Habán²⁴ found, in 1935, that the most extensive liver lesions in animals rendered toxic by the administration of thyroid preparations were in those where intercurrent infection oc-

*It is interesting that Davis and Whipple's¹⁸ experiments were suggested by Hunt's²⁹ observation that the administration of thyroid preparations exercises a protective action against acetonitrile poisoning. As stated above, they concluded that it neither protected the liver against chloroform poisoning nor apparently increased the amount of damage done by the anesthetic.

cured.* In 1941, Sealy⁴⁴ found that when animals infected with Shope's papilloma were given thyroid extract, liver changes developed, whereas, such lesions were not found in two groups of controls, one of which was receiving thyroid extract without infection with Shope's papilloma, the other being infected with Shope's papilloma but receiving no thyroid preparation.

Deleterious Effects of Anoxia.—Recent experimental work⁵³ showed that when hyperthyroid animals were exposed to artificial atmospheres containing low percentages of oxygen, degenerative lesions could usually be demonstrated in the liver, varying from slight changes when the anoxia was of short duration, to extensive degeneration when the anoxia was of longer duration. The livers of normal animals similarly exposed to anoxia showed no liver lesions. The mortality among the hyperthyroid animals was high,[†] while there were no deaths among the controls.

Since anoxemia, due to a number of causes (respiratory obstruction following operation, pulmonary edema, hyperpyrexia), is commonly encountered in hyperthyroidism,^{14, 31, 49, 62} particularly in relation to the thyroid crisis and postoperative storm, this condition may be an important etiologic factor in some of the instances where degenerative lesions are found at autopsy.

THERAPEUTIC IMPLICATIONS

Since the liver lesions associated with hyperthyroidism have been reported only in severe or long-standing cases, it is obvious that early recognition and efficient treatment of the underlying disease would largely do away with this complication. Neglected and fulminating cases of thyrotoxicosis, however, continue to be seen and it is worthwhile to consider what measures can be taken to protect the liver in such circumstances.

In the literature dealing with the general subject of liver injury, emphasis is laid on the protection afforded to the liver by certain elements of diet, notably proteins and carbohydrates.^{16, 27, 55, 56, 57} But it should be noted that however convincing the evidence in favor of the protective effect of a high protein diet against liver poisons in general, hyperthyroidism produces a new set of conditions under which the protective action of proteins may not apply. This is true also of the protective value of a high carbohydrate diet or the intravenous administration of glucose, for it must be remembered that a serious derangement of carbohydrate metabolism occurs in hyperthyroidism and that the reduced ability to store glycogen in the liver is one of the

*Schultz,⁶² in 1939, demonstrated that the myocardium of hyperthyroid animals showed lesions only when intercurrent infection was present. In the case of chronic, focal, hemolytic streptococcus infection was produced in the myocardium. Characteristic myocardial lesions were found at autopsy in these animals, whereas none were seen in the control animals. Schultz makes no reference to the liver.
[†]It has been known for some time that hyperthyroid animals tolerate anoxia poorly.^{5, 6, 67}

outstanding features of the disease. It is possibly significant that in recent investigative work it was found that neither a high protein diet nor injections of glucose were effective in protecting the livers of hyperthyroid animals against chloroform poisoning.⁵² The nutritional needs of the body, however, are enormously increased during hyperthyroidism and this fact alone, aside from any specific protective effect on the liver, is sufficient to warrant emphasis on the inclusion of adequate amounts of protein and carbohydrate in the diet of these patients.

The vitamin needs of the body are also greatly increased during hyperthyroidism and should be adequately met. That this is particularly true of the B vitamins, is suggested by Drill's work¹⁹ in this field. As already pointed out, this author reported that the B vitamins are beneficial in maintaining a normal level of liver glycogen during experimental hyperthyroidism and in later studies with Hays²⁰ demonstrated that they are of assistance in maintaining a normal dye excretion.

Since the liver under conditions of hyperthyroidism shows increased susceptibility to injury, and it is uncertain how much protection is afforded by measures that would be effective under ordinary conditions, special precautions must be taken to guard this organ from exposure to deleterious factors. In view of what has been said as to the apparent influence of intercurrent infections upon the development of liver lesions in hyperthyroidism, especial care must be taken to shield the patient from any infection. Other deleterious factors assume particular importance when an operation is to be carried out. An anesthetic should be selected that has a minimum toxic action on the liver and the greatest care should be used to see that no anoxemia results either during or subsequent to administration. In the more fulminating cases of hyperthyroidism the use of local rather than general anesthesia should receive careful consideration. During the postoperative period, if any evidence of anoxemia develops due to respiratory obstructions or pulmonary complications, prompt oxygen therapy should be instituted. It should also be remembered, as pointed out by Hartman,³³ that hyperpyrexia in itself may contribute to anoxia and the beneficial effect of oxygen therapy in the thyroid crisis, where hyperpyrexia is such a constant feature, is well recognized.^{31, 32}

REFERENCES

1. Abelin, I.: Thyroxin und Thyreoiden, *Biochem. Ztschr.* 228: 233, 1930.
2. Abelin, I.: Thyreogenes und nichtthyreogenes Jod, *Schweiz. med. Wchnschr.* 69: 1241, 1939.
3. Abelin, I., and Wehren, E.: Über das Verhalten des Schilddrüsenhormons im Tierkörper, *Arch. internat. de pharmacodyn. et de therap.* 61: 156, 1940.
4. Althausen, T. L., and Wever, G. K.: Galactose Tolerance in Hyperthyroidism, *J. Clin. Investigation* 16: 257, 1937.
5. Asher, L., and Duran, M.: Beiträge zur Physiologie der Drüsen. 44. Das Verhalten von normalen, mit Schilddrüsensubstanz gefütterten und schilddrüsenlosen Ratten gegen reinen Sauerstoffmangel, *Biochem. Ztschr.* 106: 254, 1920.

6. Barach, A. L., Eekman, M., and Molomut, N.: Modification of Resistance to Anoxia, With Especial Reference to High Altitude Flying, *Am. J. M. Sc.* 202: 336, 1941.
7. Bartels, E. C.: Liver Function in Hyperthyroidism as Determined by the Hippuric Acid Test, *Ann. Int. Med.* 12: 652, 1938.
8. Bayley, R. H.: Thyroid Crisis, *Surg., Gynec. & Obst.* 59: 41, 1934.
9. Beaver, D. C., and Pemberton, J. deJ.: The Pathologic Anatomy of the Liver in Exophthalmic Goiter, *Ann. Int. Med.* 7: 687, 1933.
10. Boyce, F. F., and McFetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test; II. Thyroid Disease, *Arch. Surg.* 37: 427, 1938.
11. Boyce, F. F., and McFetridge, E. M.: So-called "Liver Death"; a Clinical and Experimental Study, *Arch. Surg.* 31: 105, 1935.
12. Cameron, G. R., and Karunaratne, W. A. E.: Liver Changes in Exophthalmic Goitre, *J. Path. & Bact.* 41: 267, 1935.
13. Coggeshall, H. C., and Greene, J. A.: The Influence of Desiccated Thyroid Gland, Thyroxin, and Inorganic Iodine, Upon the Storage of Glycogen in the Liver of the Albino Rat Under Controlled Conditions, *Am. J. Physiol.* 105: 103, 1933.
14. Cole, W. H., and Brunner, R.: Anesthesia in Thyroidectomy for Thyrotoxicosis, *Surg., Gynec. & Obst.* 70: 211, 1940.
15. Cramer, W., and Krause, R. A.: Carbohydrate Metabolism in Its Relation to the Thyroid Gland; the Effect of Thyroid Feeding on the Glycogen Content of the Liver and on the Nitrogen Distribution in the Urine, *Proc. Roy. Soc., London, s. B.* 86: 550, 1913.
16. Davis, N. C., and Whipple, G. H.: The Influence of Fasting and Various Diets on the Liver Injury Effected by Chloroform Anesthesia, *Arch. Int. Med.* 23: 613, 1919.
17. Dinsmore, R. S.: Factors Influencing Morbidity in Thyroid Surgery, *J. A. M. A.* 109: 179, 1937.
18. Dresel, K., and Goldner, M.: Ein neuer biologischer Test für Schilddrüsenstoffe, *Verhandl. d. deutsch. Gesellsch. f. inn. Med., Kong.* 41: 534, 1920.
19. Drill, V. A.: The Effect of Yeast on the Liver Glycogen of White Rats During Hyperthyroidism, *J. Nutrition* 14: 355, 1937.
20. Drill, V. A., and Hays, H. W.: Hyperthyroidism and Liver Function in Relation to B Vitamins, *Proc. Soc. Exper. Biol. & Med.* 43: 450, 1940.
21. Eder, M. D.: Three Cases of Jaundice Occurring in Persons Suffering From Exophthalmic Goitre, *Lancet* 1: 1758, 1906.
22. Farrant, R.: Hyperthyroidism: Its Experimental Production in Animals, *Brit. M. J.* 2: 1363, 1913.
23. Foss, H. L., Hunt, H. F., and McMillan, R. M.: The Pathogenesis of Crisis and Death in Hyperthyroidism, *J. A. M. A.* 113: 1090, 1939.
24. Gerlei, François: Nécrose du foie consécutive à l'empoisonnement par la thyroxine, *Ann. d'anat. path.* 10: 555, 1933.
25. Goodpasture, E. W.: The Influence of Thyroid Products on the Production of Myocardial Necrosis, *J. Exper. Med.* 34: 407, 1921.
26. Goodpasture, E. W.: Myocardial Necrosis in Hyperthyroidism, *J. A. M. A.* 76: 1545, 1921.
27. Goldschmidt, S., Vars, H. M., and Ravdin, I. S.: The Influence of the Food Stuff Upon the Susceptibility of the Liver to Injury by Chloroform and the Probable Mechanism of Their Action, *J. Clin. Investigation* 18: 277, 1939.
28. Habán, György: Leberveränderungen bei experimentellem Hyperthyreoidismus, *Beitr. z. path. Anat. u. z. allg. Path.* 95: 573, 1935.
29. Habán, György: Über die Leberveränderungen bei Morbus Basedowii mit besonderer Berücksichtigung der Lebercirrhose, *Beitr. z. path. Anat. u. z. allg. Path.* 92: 88, 1933.
30. Habershon, S. O.: Exophthalmic Goitre; Heart Disease; Jaundice; Death, *Lancet* 1: 510, 1874.
31. Haines, S. F., and Boothby, W. M.: Oxygen Treatment With Special Reference to Treatment of Complications Incident to Goiter, *Am. J. Surg.* 7: 174, 1929.
32. Haines, S. F., Magath, T. B., and Power, M. H.: The Hippuric Acid Test in Hyperthyroidism, *Ann. Int. Med.* 14: 1225, 1941.
33. Hartman, F. W.: Lesions of the Brain Following Fever Therapy; Etiology and Pathogenesis, *J. A. M. A.* 109: 2116, 1937.
34. Hashimoto, H.: The Heart in Experimental Hyperthyroidism With Special Reference to Its Histology, *Endocrinology* 5: 579, 1921.

35. Heilmeyer, L.: Blutfarbstoffwechselstudien; Blutmauserung und Leberfunktion beim Morbus Basedow, *Deutsches Arch. f. klin. Med.* 171: 515, 1931.
36. Hewitt, J. A.: The Effect of Administration of Small Amounts of Thyroid Gland on the Size and Weight of Certain Organs in the Male White Rat, *Quart. J. Exper. Physiol.* 12: 347, 1920.
37. Higgins, G. M.: Experimental Pathology of the Liver; XII. Effects of Feeding Desiccated Thyroid Gland on Restoration of the Liver, *Arch. Path.* 16: 226, 1933.
38. Hoskins, E. R.: The Growth of the Body and Organs of the Albino Rat Affected by Feeding Various Ductless Glands (Thyroid, Thymus, Hypophysis, and Pineal), *J. Exper. Zool.* 21: 295, 1916.
39. Hunt, R.: The Influence of Thyroid Feeding Upon Poisoning by Acetonitrile, *J. Biol. Chem.* 1: 33, 1906.
40. Kerr, W. J., and Rusk, G. Y.: Acute Yellow Atrophy Associated With Hyperthyroidism, *M. Clin. North America* 6: 445, 1922.
41. Kohn, L. W.: Gastrointestinal Symptoms in Disturbances of the Thyroid, *N. York M. J.* 110: 1066, 1919.
42. Kuriyama, S.: The Influence of Thyroid Feeding Upon Carbohydrate Metabolism, *Am. J. Physiol.* 43: 481, 1917.
43. Kuriyama, S.: The Influence of Thyroid Feeding Upon Carbohydrate Metabolism; I. The Storage and Mobilization of the Liver Glycogen in Thyroid-fed Animals, *J. Biol. Chem.* 33: 193, 1918.
44. Lahey, F. H.: The Reduction of the Mortality in Hyperthyroidism, *New England J. Med.* 213: 475, 1935.
45. Lewis, W.: Hyperthyroidism and Associated Pathology, *Am. J. M. Sc.* 181: 65, 1931.
46. Lichtman, S. S.: Liver Function in Hyperthyroidism, With Special Reference to the Galactose Tolerance Test, *Ann. Int. Med.* 14: 1199, 1941.
47. Lichtman, S. S.: Liver Function in Hyperthyroidism, *Arch. Int. Med.* 50: 721, 1932.
48. Lord, J. W., Jr., and Andrus, W. deW.: Changes in the Liver Associated With Hyperthyroidism, With a Study of Plasma Prothrombin Levels in the Immediate Postoperative Period, *Arch. Surg.* 42: 643, 1941.
49. Maddock, W. G., Pedersen, S., and Coller, F. A.: Studies of the Blood Chemistry in Thyroid Crisis, *J. A. M. A.* 109: 2130, 1937.
50. Marine, D., and Lenhart, C. H.: Pathological Anatomy of Exophthalmic Goiter: The Anatomical and Physiological Relations of the Thyroid Gland to the Disease; the Treatment, *Arch. Int. Med.* 8: 265, 1911.
51. McIver, M. A.: Increased Susceptibility to Chloroform Poisoning Produced in the Albino Rat by Injection of Crystalline Thyroxin, *Proc. Soc. Exper. Biol. & Med.* 45: 201, 1940.
52. McIver, M. A., and Winter, E. A.: Further Studies on Increased Susceptibility to Chloroform Poisoning Produced in the Albino Rat by Injection of Crystalline Thyroxin, *J. Clin. Investigation* 21: 191, 1942.
53. McIver, M. A., and Winter, E. A.: Deleterious Effects of Anoxia on the Liver of the Hyperthyroid Animal, *Arch. Surg.* (In press.)
54. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, 1937, J. B. Lippincott Company, p. 292.
55. Miller, L. L., and Whipple, G. H.: Chloroform Liver Injury Increases as Protein Stores Decrease; Studies in Nitrogen Metabolism in These Dogs, *Am. J. M. Sc.* 199: 204, 1940.
56. Moise, T. S., and Smith, A. H.: Diet and Tissue Growth; I. The Regeneration of Liver Tissue on Various Adequate Diets, *J. Exper. Med.* 40: 13, 1924.
57. Opie, E. L., and Alford, L. B.: The Influence of Diet on Hepatic Necrosis and Toxicity of Chloroform, *J. A. M. A.* 62: 895, 1914.
58. Pemberton, J. deJ.: Reactions Following Operations for Hyperthyroidism, *Ann. Surg.* 104: 507, 1936.
59. Raab, W., and Terplan, C.: Morbus Basedowii mit subakuter Leberatrophie, *Med. Klin.* 19: 1154, 1923.
60. Salter, W. T.: The Endocrine Function of Iodine, Cambridge, Mass., 1910, Harvard University Press, p. 201.
61. Schmidt, C. R., Walsh, W. S., and Chesky, V. E.: Liver Insufficiency in Toxic Goiter and Its Treatment, *Surg., Gynec. & Obst.* 73: 502, 1911.
62. Schnedorf, J. G., McClure, R. D., and McGraw, A. B.: Rationale and Use of Oxygen in the Postoperative Treatment of Hyperthyroidism, *Surg., Gynec. & Obst.* 72: 26, 1941.
63. Schultz, M. P.: The Induction of Carditis by the Combined Effects of Hyperthyroidism and Infection, *Pub. Health Rep.* 51: 1267, 1939.

64. Sealy, W. C.: The Induction of Liver Necrosis in Rabbits by the Combination of Experimental Hyperthyroidism and Shope Papilloma, *Ann. Surg.* 113: 572, 1941.
65. Shaffer, J. M.: Disease of the Liver in Hyperthyroidism, *Arch. Path.* 29: 20, 1940.
66. Simonds, J. P., and Brandes, W. W.: The Effect of Experimental Hyperthyroidism and of Inanition on the Heart, Liver and Kidneys, *Arch. Path.* 9: 445, 1930.
67. Streuli, H., and Asher, L.: Beiträge zur Physiologie der Drüsen. 36. Das Verhalten von schilddrüsenlosen, milzlosen, schilddrüsen und milzlosen Tieren bei O₂-Mangel, zugleich ein Beitrag zur Theorie der Bergkrankheit, *Biochem. Ztschr.* 87: 359, 1918.
68. Sutcliffe, E. H., and Durh, M. B.: An Extraordinarily Acute Case of Graves's Disease, *Lancet* 1: 717, 1898.
69. Weller, C. V.: Hepatic Pathology in Exophthalmic Goiter, *Ann. Int. Med.* 7: 543, 1933.
70. Youmans, J. B., and Warfield, L. M.: Liver Injury in Thyrotoxicosis as Evidenced by Decreased Functional Efficiency, *Arch. Int. Med.* 37: 1, 1926.
71. Zavadovsky, B., and Azimov, G.: Zur Frage der Feststellung von Thyroxin im Organismus hyperthyreoidisierter Säugetiere, *Arch. f. d. ges. Physiol.* 216: 65, 1927.

Review of Recent Meetings

MEETING OF THE AMERICAN SURGICAL ASSOCIATION, APRIL 6-8, 1942, CLEVELAND, OHIO

J. DEWEY BISGARD, M.D., OMAHA, NEB.

ADDRESS of the President, Harvey B. Stone, Baltimore.—Homeostasis demands a constant defense against (1) trauma, (2) parasites, (3) psychic and emotional influences (in man), and it also demands the maintenance of body economy. Cancer represents an escape from normal restraints, a breakdown of homeostasis. The mechanisms of defense are (1) encysting, (2) suppurative, (3) immune bodies, and (4) antiphylactic reaction. Cross grafting in higher forms of life is defeated by host defense reaction. The graft is already adapted to the habitat from which it is removed and unable to adapt itself to its host which reacts against it. The fundamental factor may be the genes which determine specificity, or simply the reaction to protein molecules. Grafting or replacement surgery is an enormous unexplored field. It is within the realm of possibility in the future to transplant from one individual to another not only vital organs but even extremities. For successful transplanting of tissue such as thyroid it is necessary to (1) use small transplants, (2) obtain complete hemostasis and use strict aseptic and atraumatic technique, (3) be assured of good blood supply in the recipient bed, (4) (?) physiologic need of transplant, (5) (?) placement of graft into its natural region.

The Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in the Embryo, B. H. Willer (by invitation), Chicago.—All pigment cells for the skin, hair, and feathers migrate in the embryo from the neurocrest cells. Transplants from the neurocrest of pigmented breeds of chick embryos, such as black leghorns, to the site of the wing bud of embryos of nonpigmented breeds, such as white leghorns, caused these latter chicks to grow a wing with black feathers and vice versa. These transplanted melanophores are affected by such hormones as estrin, thyroid extract, and desoxycorticosterone. These substances profoundly influenced the color of the feathers. Melanophores from the white breeds produce no color because they die early; this explains the graying of hair in man. Premature graying represents premature death of melanophores, either on a familial or a hormonal basis.

Studies in the Free Transplantation of Skin, James Barrett Brown, St. Louis.—Epithelization of donor sites of split skin grafts has been found to occur within six days with new squamous epithelium "dedifferentiating" from the remnants of follicles deep in the derma. If the healing stimulus is low, epithelization of any defect in the skin is retarded. Fibroplasia is also retarded so that there is less contracture. When large burned defects heal by "scar" epithelium there are fissuring and breaks in the epithelium with excitation of the healing stimulus over a long period of time which may result in malignant degeneration. The progression of this benign proliferative activity of the epithelium to a malignant invasive one was demonstrated.

Homografts have been observed to survive in identical twins. Under other circumstances they persist for a few weeks and then are lost. Their use as emergency dressings for burns was demonstrated. They were used simply to cover the surfaces until they were replaced by the patient's own epithelium.

Clinical and Experimental Studies in the Treatment of Burns, Vinton E. Siler (by invitation), and **Mont R. Reid, Cincinnati**—Evidence from both clinical and animal studies was presented that compression dressings over burned surfaces reduces the loss of plasma from those surfaces, thereby conserving plasma and diminishing thermal shock. These dressings are applied after the surfaces have been meticulously cleansed with rigid aseptic technique and then covered with vaselined gauze. The burned areas are put at rest and the extremities splinted or encased in plaster of Paris. Subsequent dressings were done infrequently. Often second degree burns were healed at first redressment. In 145 cases so treated there were five deaths and in these five over 40 per cent of the skin surface was burned.

In the discussion, **W. G. Penfield, Montreal**, stated that the care of burns was the biggest problem of the War in Britain. **S. L. Koch, Chicago**, reported 480 cases of burns with 39 per cent mortality using the technique of cleansing with copious washing with saline solution, débridement, vaseline gauze dressings with compression, immobilization in splints, and adequate plasma and other shock therapy. He believes that this method with slight modification could be used in military surgery. **L. Elloesser, San Francisco**, and **E. Young, Rochester, N. Y.**, reported experiences with and recommended immediate excision of areas burned to third degree and covering these areas with split grafts immediately. With takes the areas are covered with skin within a few days and infection and contractures avoided.

Chronic Infected Burns With Hemorrhage, William A. Altemeier (by invitation), and **B. N. Carter, Cincinnati**—In three cases in which bleeding had persisted in spite of all forms of treatment, the oozing stopped promptly and permanently following applications of zinc peroxide. From only one of these cases how ever were anaerobes cultured.

In the discussion, **F. L. Meleney, New York**, stated that anemia in infected burn cases resulted from hemolytic activity as well as capillary bleeding, and that symbiotic infections including anaerobes were prone to cause capillary oozing.

Procurement and Use of Blood Substitutes in the Army, Douglas B. Kendrick, Jr., Major, M. C., U. S. A. (by invitation)—The Red Cross operates eighteen blood donor stations throughout the country where blood is taken from 1,500 volunteers daily. For the service, plasma is packaged in both dry and wet forms. There is available over 250,000 units of dried plasma. From its use there have been only 2 per cent reactions and none severe. Recently, the albumin fraction has been extracted from plasma and packaged in 25 per cent solutions in smaller bulk to facilitate storage and shipping. Fifty cubic centimeters have an osmotic pull of 250 c.c. of plasma.

The Problem of Intestinal Gases Complicating Abdominal Surgery, Albert O. Singleton, Galveston—A study of intestinal gases shows that they are composed mainly of swallowed air. Experimental evidence was given which indicated that distention of the intestine seriously modifies its normal function, resulting in disturbance of electrolytic balance in the blood, as well as seriously interfering with the circulation of the bowel. A clinical study of gastric suction as compared to duodenal suction indicates that in the former there is very little fluid lost, while in the latter there is a great deal of fluid lost. Postoperative ileus is of little consequence in the absence of distention, the return of peristalsis following abdominal operations is much more prompt if gases are not allowed to enter the intestine, the loss of fluids and electrolytes by gastric suction is small in amount and can be easily replaced by parenteral methods, one of the greatest adjuncts to abdominal surgery for the comfort of the patient and the lowering of mortality is the use of gastric suction to prevent intestinal distention.

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Since air is swallowed during induction of anesthesia the stomach should be intubated and aspirated before and during operation.

In the discussion, **W. D. Gatch**, Indianapolis, reminded the group that distention causes atelectasis and anoxia by elevating the diaphragm and limiting its excursion. **A. O. Whipple**, New York, stated that ileus may be caused by edema of the bowel resulting from hypoproteinememia and overhydration. Intestinal intubation is desirable in conjunction with resection of the right colon. **F. A. Collier**, Ann Arbor, stated that much air is swallowed during the excitement stage of anesthesia. **W. G. Maddock**, Ann Arbor, believes that much air may enter the stomach without being swallowed.

Small Intestinal Distention: A Study of Five Years' Treatment, **Charles G. Johnston**, and **R. J. Noer** (by invitation), Detroit—This study of a series of cases with small bowel distention showed that decompression with suction applied through a tube indwelling the stomach, duodenum, or (particularly) the small bowel down to the level of the obstruction is an invaluable aid as an adjunct to other methods of treating intestinal distention and obstruction. It was curative alone in some cases. Its use, however, demands greater accuracy of diagnosis, particularly in respect to recognition of strangulation. It facilitates operation and postoperative care. Immediate or early operation should be done in every case in which the possibility of strangulation cannot be excluded.

New Operative Techniques in the Management of Bowel Obstruction, **Owen H. Wangensteen**, Minneapolis—A definite, general lowering of the mortality of obstruction came about largely through development of nonoperative decompressive measures. Further reduction of the mortality awaits development of improved methods of dealing with the obstructed bowel surgically, by employment of primary resection and closed anastomosis in nonviable intestinal strangulations, and development of operative means of decompressing the distended bowel aseptically.

The intestine is perforated with a trocar containing a catheter fitted to a suction system. The bowel is emptied without soiling by pleating it over the catheter.

In the discussion, **L. S. McKittrick**, Boston, stated that nonoperative decompression has caused disastrous delay in certain cases and that immediate operation is indicated in all cases in which strangulation cannot be excluded. **Dr. Wangensteen**, in closing, stated that rebound tenderness was indicative of strangulation.

Experiences With the Surgical Management of Diverticulitis of the Sigmoid, **R. H. Smithwick**, Boston—An analysis was made of sixty cases operated upon for diverticulitis and associated complications including acute perforation, localized abscess, vesicosigmoidal fistula, and external fistula, as well as subacute and chronic nonperforated lesions. The sigmoid was resected in thirty cases, employing four different techniques. Included with other methods of treatment were simple drainage and temporary colostomy. The mortality from resection was low and the ultimate results in the resected group were superior to those of the group treated more conservatively.

In the discussion, **H. W. Cave**, New York, stated a preference for radical resection and this by the exteriorization or Mikulicz type of operation. He stressed the frequency with which these lesions are explored and even resected upon a diagnosis of carcinoma.

Surgical Treatment of Malignant Lesions of the Sigmoid With Extension, **Ralph F. Bowers**, New York—Four cases in which carcinoma of the sigmoid had infiltrated the bladder and in which the involved portions of the bladder had been resected along with the sigmoid were reported. In one case the entire bladder, prostate, and seminal vesicles were removed after transplanting the ureters to the colon. In this series the results of long cures have justified the radical nature of the operations.

In the discussion, V. C. David, Chicago, reported six personal cases in which portions of the bladder were excised and long periods of "cure" obtained. R. B. Cattell, Boston, stated that a preliminary transverse colostomy should be done and resection or drainage delayed. R. K. Gilchrist, Chicago, stated that studies of several resected specimens had failed to show carcinomatous infiltration of the bladder but rather that the fixation and fistulas were inflammatory.

The Operative Repair of Massive Rectal Prolapse, Roscoe R. Graham, Toronto—Inasmuch as rectal prolapse is in reality a sliding hernia of the pouch of Douglas it should be treated as a hernia, applying the principles utilized in the repair of hernias elsewhere. An operation was described following these principles, namely, dissection and disposal of the sac, the extended peritoneal lining of the pouch of Douglas, and closure of the defect in the supporting levator ani muscles. Three cases so treated with good results were reported.

The Effect of Pneumonectomy Upon Cardiac Pulmonary Function in Adults, Andre Cournand (by invitation), and Frank B. Berry, New York—From a study of pulmonary efficiency of the remaining lung and of cardiac efficiency following pneumonectomy in twelve cases, it was found that distention of emphysema of the remaining lung did not increase its efficiency but rather decreased it. Prevention or reduction of overdistention by means of thoracoplasty following pneumonectomy increased the efficiency as measured by methods of evaluating ventilatory function, efficiency of gas exchange, and cardiac reserve. In a few cases dyspnea persisting many months after pneumonectomy was relieved following thoracoplasty.

In the discussion, E. A. Graham, St. Louis, stated that he had followed pneumonectomy by thoracoplasty in his earlier cases believing it necessary to help obliterate the empty cavity. Reinhoff's observations led him to abandon the procedure. He questioned the advisability of increasing the magnitude of the operation by immediately supplementing a thoracoplasty. In closing, Dr. Berry stated that they had found studies of oxygen saturation of the blood very helpful in determining the cause of dyspnea.

A Practical Consideration of Open Pneumothorax Under Sodium Evipal, Sodium Pentothal, and Ether Anesthesia, C. A. Moyer, J. B. McKittrick (by invitation), and Frederick A. Collier, Ann Arbor—Under evipal and pentothal anesthesia dogs with induced pneumothorax developed expiratory predominance which persisted after termination of the pneumothorax. In two animals artificial respiration failed to re-establish normal breathing.

The predominance of expiratory activity instituted by open pneumothorax during moderate evipal and pentothal anesthesia has not been seen during moderate ether anesthesia. This finding coupled with the observation that hypercarbia and anoxia increase the toxicity of evipal and pentothal indicates that ether is superior to evipal and pentothal for anesthetizing persons suffering from penetrating wounds of the chest.

Clinical and Experimental Observations on the Closure of the Bronchus Following Total Pneumonectomy, William F. Reinhoff, Jr., James Gannon, Jr. (by invitation), and Irwin Sherman, Baltimore—Leakage from the bronchial stump constitutes one of the major hazards following pneumonectomy. An extensive experimental study in animals and observations made in sixty one cases subjected to pneumonectomy have indicated that the bronchial stump is most securely closed by placing two rows of interrupted sutures, the proximal one to relieve tension without strangulation and the distal row to accomplish approximation. Silk sutures are preferable. Much added security is gained by covering the stump with an adjacent flap or pedicle flap of pleura. In the sixty one cases the bronchus opened in sixteen, or 26 per cent, and this caused death in three.

In the discussion, E. A. Graham, St. Louis, stated that he had sutured free, as well as pedicle, grafts of pleura over the stump. N. S. Shenstone, Toronto demonstrated a method of closure of the stump in which the bronchus was crushed and ligated proximal to the suture line. A. Ochsner, New Orleans, stated that in a series of thirty two pneumonectomies the bronchial stump opened in three and in two of these x ray therapy had been given preoperatively.

Transthoracic Resection of Tumors of the Esophagus and Stomach, Edward D. Churchill, and Richard H. Sweet (by invitation), Boston—In a series of twenty one cases of carcinoma of the mid portion of the esophagus, nine were resectable and of these, three survived and are living and well. They were resected by a modified Torek operation. An equal series of carcinomas of the distal one third of the esophagus and cardia of the stomach were presented. In 23 per cent there were metastatic glands below the diaphragm along the lesser curvature indicating necessity of preliminary laparotomy. Resection was accomplished through a left thoracotomy wound. Since the esophagus has no serosa, accurate approximation of the mucosa in the anastomosis is essential.

In the discussion, D. B. Phemister, Chicago, reported twelve cases, with eight immediate survivors. There were seven of the lower third and cardia, with three survivors. A. Ochsner, New Orleans, stated a preference for the two stage operation dividing the gastrophrenic omentum through the preliminary laparotomy wound and prefers the right thoracotomy approach for resection. It is important to anchor the stomach when it is drawn up through the incised diaphragm.

The Use of Oxygen in the Treatment of Transudation and Exudation Into the Lungs, Cecil K. Drinker (by invitation), Boston—The lungs have rich lymphatic systems which drain into the right innominate vein. In presence of anoxia there is increased flow of lymph from the lungs and an increased permeability of the capillaries. Obstructed and forced breathing increases the flow of lymph and with anoxia, lymph exudes into the alveoli and interstitial spaces. This coating of lymph prevents air from reaching the capillaries and makes resuscitation impossible. Early recognition of disturbance of lymphatic flow and prevention of its exudation by prompt relief of obstructed and forced breathing and the administration of oxygen must be done before the irreversible stage is reached.

The Treatment of Metastatic Cancer of the Prostate, Charles Huggins, Chicago—In many instances cancer of the prostate is very sensitive to hormonal changes. Castration in thirty one out of forty five cases caused moderate to complete regression of the neoplasm, including both local and metastatic lesions. Stilbestrol and x radiation of the testes also cause regression, whereas testosterone causes an increase in the growth of the tumor, and in pain and other symptoms.

The prostate normally contains acid phosphatase. This is much increased with carcinoma as is the blood acid phosphatase. An increase of acid phosphatase of the blood is diagnostic of carcinoma of the prostate. Just as castration and stilbestrol cause regression of the neoplasm they decrease the blood acid phosphatase, and, conversely, testosterone increases it.

Cases with extensive bony metastases were presented showing amazing temporary cures with relief of all symptoms and disappearance of all evidence of the neoplasm following castration.

Reflexes Originating in the Common Duct Giving Rise to Pain Simulating Angina Pectoris, I. S. Ravdin, and H. P. Royster (by invitation), Philadelphia—Pseudo angina can arise from lesions in the common bile duct. The attacks of pain, while classical of angina pectoris, are prone to come on at rest in bed at night and are not associated with an effort syndrome. They may present electrocardiographic evidence of coronary disease which disappears as do the symptoms after surgical relief of the lesion of the common duct. Stimuli arising in the common

duct cause, in these cases, reflex spasm of the coronary arteries. There may or may not be intrinsic coronary disease with the superimposed spasm.

In two cases relieved of anginoid pain by removal of stones from the common bile duct the authors were able to elicit the same pain after operation by distending the common bile duct by injections through the T tube.

In the discussion, C. G. Mixter, Boston, reported three cases relieved of residual postcholecystectomy colic following lower dorsal sympathectomy. G. J. Heuer, New York, presented statistical data showing that there is a higher incidence of hypertension and cardiorenal disease in people with gall bladder disease than in those of the same age without this disease. J. A. Wolfer, Chicago, cited a case with the reverse situation, that is, coronary thrombosis with symptoms of gall bladder colic and a normal gall bladder. He also presented a case with a diaphragmatic hernia which gave rise to symptoms and electrocardiographic evidence of coronary disease.

Tests of Hepatic and Pancreatic Function in the Differential Diagnosis and Preparation of Patients With Lesions of the Biliary Tract, William D. Andrus (by invitation), Jere W. Lord, Jr., and Michael Lake, New York.—The level and the response toward normal in prothrombin time to the parenteral administration of vitamin K is a guide to the functional status of the liver. By an analysis of the duodenal contents for the presence or absence and character of pancreatic ferments it is possible to determine the presence or absence of a concomitant obstruction of the pancreatic duct in jaundiced patients. Yeast contains a factor which aids in protection and regeneration of the liver as do carbohydrates, proteins, and choline. Avoidance of anoxia, which is very deleterious to the liver, is important.

In the discussion, I. S. Ravdin, Philadelphia, stated the simple truth that tissues can be built in regeneration only from proteins. Carbohydrates are essential to this process but aid only as protein sparing substances. The best proteins for purposes of regeneration are the proteins of the liver itself. Cystine does give some protection to the liver.

Vitallium Tubes in Biliary Surgery, Herman E. Pearse, Rochester, N. Y.—In construction of bile ducts it is very desirable to preserve the sphincter of Oddi and so prevent regurgitation from the duodenum. Vitallium tubes for permanent bridging of defects in the common and hepatic ducts were demonstrated. These included a variety of design such as Y tubes to meet the various circumstances which might be encountered and a small tube for repair of chronic pancreatic fistulas. A few illustrative cases with very satisfactory results were presented.

In the discussion, H. M. Clute, Boston, reported one case with a satisfactory result. E. W. Rockey, Portland, reported satisfactory results in experimental animals with metallic magnesium tubes. W. G. Maddock, Ann Arbor, reported his experiences with the tubes in two cases, both unsatisfactory, followed by chills, fever, and icterus.

Carcinoma of the Pancreas and Ampullary Region, With Report of Six Additional Cases, Samuel C. Harvey, and Ashley W. Oughterson, New Haven.—Two cases were reported in which the body of the pancreas was resected for carcinoma, and two cases in which the head of the pancreas and the duodenum were resected for carcinoma.

In the discussion, A. O. Whipple, New York, reported a recently collected series of sixty four cases of resection of the duodenum and head of pancreas. Of these, 35 per cent were done in one stage. Two cases followed over two years have shown no ill effect from loss of pancreatic juices; both can take 80 per cent of the normal amount of fat without digestive disturbance. T. G. Orr, Kansas City, and V. C. Hunt, Los Angeles, reported their experiences with four and five cases, respectively.

In the discussion, **E. A. Graham**, St. Louis, stated that he had sutured free, as well as pedicle, grafts of pleura over the stump. **N. S. Shcnstone**, Toronto, demonstrated a method of closure of the stump in which the bronchus was crushed and ligated proximal to the suture line. **A. Ochsner**, New Orleans, stated that in a series of thirty-two pneumonectomies the bronchial stump opened in three and in two of these x-ray therapy had been given preoperatively.

Transthoracic Resection of Tumors of the Esophagus and Stomach, **Edward D. Churchill**, and **Richard H. Sweet** (by invitation), Boston.—In a series of twenty-one cases of carcinoma of the mid-portion of the esophagus, nine were resectable and of these, three survived and are living and well. They were resected by a modified Torek operation. An equal series of carcinomas of the distal one-third of the esophagus and cardia of the stomach were presented. In 23 per cent there were metastatic glands below the diaphragm along the lesser curvature indicating necessity of preliminary laparotomy. Resection was accomplished through a left thoracotomy wound. Since the esophagus has no serosa, accurate approximation of the mucosa in the anastomosis is essential.

In the discussion, **D. B. Phemister**, Chicago, reported twelve cases, with eight immediate survivors. There were seven of the lower third and cardia, with three survivors. **A. Ochsner**, New Orleans, stated a preference for the two-stage operation dividing the gastrohepatic omentum through the preliminary laparotomy wound and prefers the right thoracotomy approach for resection. It is important to anchor the stomach when it is drawn up through the incised diaphragm.

The Use of Oxygen in the Treatment of Transudation and Exudation Into the Lungs, **Cecil K. Drinker** (by invitation), Boston.—The lungs have rich lymphatic systems which drain into the right innominate vein. In presence of anoxia there is increased flow of lymph from the lungs and an increased permeability of the capillaries. Obstructed and forced breathing increases the flow of lymph and with anoxia, lymph exudes into the alveoli and interstitial spaces. This coating of lymph prevents air from reaching the capillaries and makes resuscitation impossible. Early recognition of disturbance of lymphatic flow and prevention of its exudation by prompt relief of obstructed and forced breathing and the administration of oxygen must be done before the irreversible stage is reached.

The Treatment of Metastatic Cancer of the Prostate, **Charles Huggins**, Chicago.—In many instances cancer of the prostate is very sensitive to hormonal changes. Castration in thirty-one out of forty-five cases caused moderate to complete regression of the neoplasm, including both local and metastatic lesions. Stilbestrol and x-radiation of the testes also cause regression, whereas testosterone causes an increase in the growth of the tumor, and in pain and other symptoms.

The prostate normally contains acid phosphatase. This is much increased with carcinoma as is the blood acid phosphatase. An increase of acid phosphatase of the blood is diagnostic of carcinoma of the prostate. Just as castration and stilbestrol cause regression of the neoplasm they decrease the blood acid phosphatase, and, conversely, testosterone increases it.

Cases with extensive bony metastases were presented showing amazing temporary cures with relief of all symptoms and disappearance of all evidence of the neoplasm following castration.

Reflexes Originating in the Common Duct Giving Rise to Pain Simulating Angina Pectoris, **I. S. Ravdin**, and **H. P. Royster** (by invitation), Philadelphia.—Pseudo-angina can arise from lesions in the common bile duct. The attacks of pain, while classical of angina pectoris, are prone to come on at rest in bed at night and are not associated with an effort syndrome. They may present electrocardiographic evidence of coronary disease which disappears as do the symptoms after surgical relief of the lesion of the common duct. Stimuli arising in the common

In the discussion, **Cox**, stated that amino acids regenerate plasma proteins equally well when administered by either oral or intravenous routes. **O. H. Wangenstein**, Minneapolis, said that surgeons must become more alert to the importance of nitrogen metabolism and the protein needs of surgical cases. The administration of amino acids causes little or no regeneration of plasma proteins because they are immediately utilized. **R. Elman**, St. Louis, stated that the colloidal property of amino acids was about the same as that of glucose and much less than that of plasma. In closing, **A. Brunschwig**, Chicago, stated that the use of amino acids was contraindicated in cases with damaged livers. Severe reactions occur in these cases. Casein can be given subcutaneously in 3 per cent solutions of distilled water.

The Nature and Functions of the Various Plasma Proteins and Other Possible Therapeutic Uses, **Edwin J. Cohn** (by invitation), Boston.—Plasma can be fractionated and the individual fractions utilized separately. The water-holding protein molecules of albumin exert approximately 80 per cent of the osmotic pull of whole plasma. Almost pure crystalline human albumin has been isolated and packaged in 25 per cent solutions for use of the armed forces. The albumin fraction of bovine plasma is almost identical to that of human plasma in its physiochemic properties and should be well tolerated by man. It is now undergoing clinical trial. As by-products of fractionations of the large quantity of plasma used in the study of human albumin, pure fibrinogen, thrombin, and prothrombin have been prepared and studied. When these fractions have been applied to oozing surfaces, bleeding has stopped almost instantaneously.

Observations on 1,000 Intravenous Injections of Hydrolyzed Casein in Post-operative Patients, **Robert Elman**, and **E. Bradley** (by invitation), St. Louis.—Out of 1,000 intravenous injections of hydrolyzed casein (Amigen*) to patients, postoperatively there were only two severe reactions (allergic). There were ten instances of chills and fever and incidence of phlebitis did not exceed that which occurs with glucose. Amigen was used in 2½ per cent and 5 per cent solution added to the glucose solution.

Recent Experiences in the Diagnosis and Treatment of Thrombophlebitis of the Lower Extremity, **Jacob Fine**, Boston.—When the occurrence of phlebitis of the femoral or iliac veins is obvious or suspected some corroborative evidence can be obtained by venography, and the site and extent of the thrombus determined. The associated spasm of the veins may simulate filling defects and lead to error in interpretation. Ligation and division of the femoral or iliac vein proximal to the thrombus prevents embolization and is indicated as a prophylactic procedure. The distal end of the vein is opened and the clot removed by aspiration. The femoral vein should be ligated proximal to the vena profunda. Several venograms demonstrating filling defects, spasm, etc., were shown and also cases in which emboli were showered repeatedly until ligation was performed above the thrombus.

In the discussion, **A. Ochsner**, New Orleans, reported ninety-one cases in which phlebitis had been promptly relieved and cured by novocain injection of the lumbar sympathetic ganglia. Only when embolization as evidenced by pulmonary infarction takes place is venography and ligation indicated and justifiable. **L. S. McKittrick**, Boston, stated that venography is inconclusive as to information and is a hazardous procedure. He favored high ligation in selected cases.

An Experimental Approach to the Problem of Menstrual Disorders, **John C. Burch**, and **Doris H. Phelps** (by invitation), Nashville.—Experimental studies were reported relative to the etiology of glandular cystic hyperplasia of the endometrium. Ovarian failure results from both intrinsic and extrinsic factors. It

*Mead Johnson & Co.

Spontaneous Internal Biliary Fistulae, Charles B. Puestow, Chicago—An experience with sixteen cases with spontaneous internal biliary fistulae was reported. These fistulae communicated with the stomach, colon, duodenum, and choledochus. There was a mortality of 19 per cent in the series. From reflux and ascending infection, several cases had severe cholangitis. Icterus may be due to this factor or to obstruction. In most instances a ray was diagnostic.

In the discussion, **H. H. Trout, Roanoke**, discussed the occurrence of obstruction of the bowel associated with fistulae, occasionally caused by large stones extruded into the gastrointestinal tract through the fistula. **J. M. T. Finney, Jr., Baltimore**, reported two cases with multiple fistulae, one with fistulae between the gall bladder and stomach and duodenum and colon and the other between the gall bladder and colon in a case with actinomycosis. **J. D. Bisgard, Omaha**, reported a case of lymphosarcoma in which the barium given by mouth filled the common duct, thus leading to an erroneous diagnosis of fistula. By retraction the tumor had rendered the duodenal end of the common duct patulous so that barium passed into it from the duodenum. The duodenum in this case was resected by a one stage Whipple operation.

Tissue Reaction to Ribbon Catgut and Preserved Ox Fascia Lata Strips, Amos R. Koontz, Baltimore—Strips of ox fascia lata, if properly prepared, have certain advantages as suture material. They cause negligible reaction in the tissues and are not absorbed until replaced by fibroblasts which readily infiltrate them. They are also soft and pliable.

In the discussion, **D. B. Phemister, Chicago**, stated that tissue reaction to catgut resulted mainly from the fluid in which it was preserved. These chemicals should be soaked out. **J. A. Key, St Louis**, found no foreign body reaction around ox fascia in experimental animals.

The Mechanism of the Action of X-ray Therapy Upon Infection, J. Dewey Bisgard, Howard B. Hunt (by invitation), Orvis A. Neely, and Paul Scott, Omaha—Evidence that in rabbits x radiation causes the liberation of a nonspecific antitoxic factor was presented. This factor was present in the peritoneal fluid and blood serum of these animals within twenty four hours after irradiation, reached a peak of effective concentration in forty eight hours, and was dissipated within seven days. This antitoxic substance caused survival of animals receiving a lethal dose of the toxins of both hemolytic *Escherichia coli* and diphtheria. When serum from irradiated animals was injected into normal stock animals a certain degree of passive immunity to these toxins resulted. This is at least in part an explanation of the beneficial effect of irradiation of infection.

In the discussion, **F. L. Meleney, New York**, stated that in addition to toxins, various chemical substances which are irritating to the tissues cause the development of nonspecific antibodies. **A. Brunswick, Chicago**, in a study of cutaneous infections in a series of animals found that x radiation reduced inflammatory reaction but did not prevent suppuration and necrosis or hasten resolution and healing.

Observations on the Loss of Nitrogen in the Immediate Postoperative Period, Alexander Brunswick, Dwight E. Clark (by invitation), and Nancy Corbin, Chicago—Results were reported of daily nitrogen balance studies during the first ten day period following major operations in forty one cases. As a result of protein catabolism there was a large negative balance (the loss of nitrogen in all excretions exceeding intake) in all cases save those in which the patients received proteins parenterally. The average daily loss in unsupported cases was 14 Gm. Several patients who received 100 c.c. of a 10 per cent solution of hydrolyzed casein daily were maintained in positive nitrogen balance much of the time. Some moderate transitory reactions occurred from the use of casein.

year or more; healed process as observed by sigmoidoscopic examination; and distensibility, adequate lumen, and absence of obstruction, as determined by barium enema. If early ileostomy is elected for ulcerative colitis, the general mortality will be lower, complications will be reduced, and fewer permanent ileostomies will be necessary. Closure should be effected by suture of ileum to ileum.

Indications for ileostomy are (1) acute fulminating type of disease, (2) failure of medical management, (3) perforation, (4) hemorrhage, (5) obstruction, and (6) polypi.

In the discussion, H. W. Cave, New York, urged earlier use of ileostomy but cautioned that it should follow only after an adequate trial of medical treatment had failed. W. E. Ladd, Boston, reported three cases of ulcerative colitis in infants less than 6 months of age. Seven children in which ileostomies have been closed have remained well.

Skin Removal in Radical Mastectomy, William Crawford White, New York.—Follow-up observations of 254 cases that had had radical mastectomies for carcinoma five and more years previously showed that local recurrences and the mortality rate were not influenced by the extent to which the skin was excised. Many developed local recurrences but death resulted from distant metastases rather than local recurrences.

REPORT OF THE MEETING OF THE AMERICAN ORTHOPEDIC ASSOCIATION, BALTIMORE, MD., JUNE 3-6, 1942

GUY A. CALDWELL, M.D., NEW ORLEANS, LA.

THE members of the Association were guests of George Bennett and associates at Johns Hopkins Hospital, Wednesday, June 3, 1942. Winthrop Phelps, Baltimore, who has done a great deal of special work on spastic paralysis, demonstrated the diagnostic and prognostic value of injecting procaine hydrochloride into spastic muscles. A few cubic centimeters of procaine hydrochloride injected into the body of the paralyzed muscle will not only relieve the spasm but will permit normal activity of the opposing group of muscles. The surgeon can thus make a pre-operative estimate of the extent of actual contracture and of the possibility of improved function in the opposing groups of muscles.

Kellogg Speed, Chicago, presented the history and slides of a patient who survived osteogenic sarcoma with numerous metastases in the lungs for approximately twenty years. Throughout this time the metastases gradually decreased in size without any particular treatment. The patient was subjected to numerous studies to ascertain, if possible, why the proved malignant tumors became stationary or regressed rather than advanced, but no satisfactory solution was found.

Henry Meyerding, Rochester, Minn., discussed spondylolisthesis. At the Mayo Clinic, between the years 1932 and 1938, there were 876 cases, 143 of which were operated upon. Analysis of the operative cases revealed that the results were excellent. The technique employed in the majority of cases consisted of exposure of the spinous processes, laminae and articular facets of the fourth and fifth lumbar vertebrae, and of the first three sacral segments. The articular facets were curetted, shavings reflected from the laminae, as in the Hibbs' procedure, and a double bone graft, taken from the tibia, was placed alongside the spinous processes which were not broken down. In addition, bone chips and shavings from the tibia were placed around the sides of the grafts to build up a rather massive lot of bone. Following operation, a simple dressing was applied and the patient allowed up with a reinforced canvas support at the end of three to six weeks.

to be ambulatory early in the treatment with good end results. He felt that the method is well adapted to a certain number of cases under suitable conditions.

Perrin Long, Baltimore, reviewed the subject of chemotherapy in the treatment of wounds. For local implantation, he advised sulfanilamide crystals of the size comparable to table salt. Sulfanilamide should be dusted over the surface of the wound; if the wound is to be closed, only light frosting of the drug is recommended. When wounds are to be left open, the drug should be sprinkled over the surface in such a way as to give the appearance of a heavy frost.

On Friday, June 5, an interesting symposium on the treatment of anterior poliomyelitis was given. Carefully analyzed end results were presented by various men to evaluate methods of treatment in various stages.

Arthur Steindler, Iowa City, discussed **Departures From the Principals of Absolute Fixation in the Treatment of Anterior Poliomyelitis** showing that absolute fixation of paralyzed extremities has many demonstrable disadvantages to both paralyzed and unparalyzed muscle.

Plato Schwartz, Rochester, N. Y., presented experimental evidence of spasticity of muscles in anterior poliomyelitis. Evidence of spasticity exists in muscles which apparently have never been affected as well as in the antagonists of the paralyzed groups. He further demonstrated relief of the spasticity after the use of hot packs over the affected muscles.

These presentations led to a discussion of the Kenny treatment in the early stage of poliomyelitis. The reports of various observers indicated that the treatment renders the patient much more comfortable, is probably most helpful in cases in which there is respiratory paralysis, and makes possible a program of early muscle training which is particularly helpful to those who are not so seriously paralyzed. It was pointed out by others, however, that some of the cases most publicized as having been actually cured were only slightly improved, as indicated by accurate muscle tests. In general, it is believed that the end results of this treatment are similar to the results obtained by the old methods of treatment. Most of the reports indicate, however, that the Kenny treatment, perhaps slightly modified, will probably be generally adopted for treating the acute stage of poliomyelitis. Patients, thus treated, will probably be more comfortable and will recuperate more rapidly but there will still be about the same proportion of cases with residual paralysis that require bracing and corrective operations.

LeRoy Abbott and associates of San Francisco, presented a moving picture demonstration of an operation for "Arthrodesis of the Wrist Joint." In it they emphasized the wide range of usefulness of this operation in paralytic conditions and arthritic processes involving the wrist joint.

Arthur G. Davis, Erie, Pa., discussed a small series of compound fractures of the extremities with large wound areas treated by careful débridement in the early hours, implantation of sulfanilamide, closure of the wound (even if skin grafts are necessary), and the application of pressure dressings similar to those used by the plastic surgeon in his routine skin grafting procedures. He demonstrated a number of forearm, hand, and leg fractures with excellent function following such treatment.

W. E. Gallie, Toronto, presented a group of fractures of the odontoid process, most of which had not been recognized until it was possible to use the laminagraph. Patients who suffered pain and in whom there was evidence of nonunion were successfully treated by the use of a bone graft and wire interposed between the spinous processes of the first and second cervical vertebrae. In these cases, the pain was relieved and a useful range of motion was retained.

Philip D. Wilson, New York, demonstrated a metal plate, properly shaped to fit the lumbosacral curve and adapted to internal fixation of the lumbosacral region. The plate extends from the spinous process of the fourth lumbar to the second sacral vertebrae and is fastened to each of them with a small bolt. After the plate is fixed in place, an osteoperiosteal graft from the tibia is placed over the denuded bone, as in other operations for spinal fusion. By this method of internal fixation the immediate postoperative pain is relieved, the period of bed treatment is shortened, the necessity for braces or fixation in plaster is eliminated, and earlier and more complete fusion is insured. Early results in twelve cases in which the operation was performed were excellent.

One of the highlights of the meeting was the visit of J. A. MacFarlane, Colonel, R.C.A.M.C., Surgical Consultant of the Canadian Active Service Force, who had been brought to this country by the Canadian government in compliance with the request of the President of the American Orthopedic Association to discuss the management of wounds encountered in modern warfare. He emphasized the importance of the immediate performance of surgical measures as the most effective means of preventing infection including gas gangrene. Chemotherapy was regarded as a valuable adjunct but he emphasized that it should not be substituted for surgical measures and could not compensate for incomplete débridement. He stressed the necessity for small, mobile, surgical units built into fast-moving trucks and so equipped that it is possible to operate within thirty to sixty minutes of arrival at a given post. The surgeons for such small units are necessarily young and strong but they must be competent in the surgery of trauma. MacFarlane approved the measures for the treatment of shock provided by the army at present in most places. He was of the opinion that the implantation of sulfonamides in the wound following débridement and repeated in subsequent dressings was probably a valuable adjunct to treatment only when adequate surgical measures were instituted early. He further emphasized the necessity of leaving all such wounds open. Infection, and particularly gas gangrene, had often resulted when attempts were made to close the wounds following débridement in the forward areas. He stated that when properly used the closed plaster method described by Trueta was proving satisfactory for most compound fractures. He advised, however, that in the case of fractures of the femur, in addition to the plaster, traction should be provided as soon as it could be adequately maintained. The use of toxoids in Canadian and British forces has proved most efficacious in the prevention of tetanus.

F. R. Hook, Captain, U.S.N., Washington, D. C., made an appeal to the assembled teachers and instructors in orthopedies in the various universities and hospitals throughout the country to make their teaching as practical and general as possible for the benefit of the men entering the army and navy medical services. He stated that particularly in the navy, men must be general surgeons and good physicians prepared to meet any emergency on board. In many instances, the working quarters on board are restricted, particularly when the ship is in action, and the treatment may have to be completed on the same ship. It appears that under existing conditions there is little opportunity for transfer of men and evacuation of the wounded. He suggested that the third- and fourth-year students should give actual treatment to the patients in the clinics and wards in order that they might be better able to perform their military duties. He felt that many of the special courses might safely be omitted in order to let the student do more practical work of the type he is likely to encounter in service.

Wallace Cole, Minneapolis, Minn., who has been serving at the American Hospital in England, presented moving pictures of "Pin Fixation in War Fractures." A number of compound fractures of the bones in the arms and legs have been treated by the two-pin method of Roger Anderson. The patients were permitted

Book Reviews

A Textbook of Neuro-Anatomy. By Albert Kuntz, M.D. Ed. 3. Pp. 518, with 307 illustrations. Philadelphia, 1942, Lea and Febiger. \$6.00.

This third edition, so completely revised that it is practically a new textbook, is one of a number of texts on neuro-anatomy which have been published recently. It is a well-balanced text for the elementary student. The figures are of the standard type without special features.

Each chapter, except the last or twenty-sixth, terminates in a summary which is brief yet sufficiently inclusive to be useful for review. The final chapter is a laboratory outline, thirty pages of which are devoted to this subject, and the final thirteen pages are clinical case reports, illustrating anatomic lesions.

Operative Surgery. By F. W. Bancroft, A.B., M.D., F.A.C.S., Associate Clinical Professor of Surgery, Columbia University, Ed. 1. Pp. 1102, with 250 illustrations, New York, 1941, D. Appleton-Century Company, Inc.

This volume, under the authorship of many well-known American surgeons writing upon subjects of their special interests, is an unusually good one. A note by the editor, F. W. Bancroft, suggests that this is the first of a number of volumes on operative surgery. The volume deals with general principles of surgical technique and abdominal surgery. There is a chapter on surgery of the esophagus and another on the mouth. *The volume, therefore, deals essentially with the alimentary canal and its appendages and the peritoneum.* In many ways, the book is a superior work and deserves to be in the hands of all who essay to do general surgery. The high light of the volume to the reviewer's way of thinking is the section on surgical manners and ethics written under the joint authorship of M. M. Stevenson and Mont R. Reid of Cincinnati.

Two of the sections in the monograph have appeared in larger monographs previously and the material here is, in a sense, the same in more concise form. There is some duplication in the effort throughout the book, which suggests a lack of editorial supervision. Three authors describe and depict operations for subphrenic abscess. A number of the illustrations fail to come up to the general standard of excellence expected of a work of this character. Indeed, it is not a little surprising that the editor did not exert his editorial prerogatives of demanding or seeing to it that only satisfactory illustrations were included. However serious these criticisms appear to be, the monograph contains so much fine material that these defects may be overlooked readily. If the volumes to come live up to the promise suggested in this one, it will be an unusual surgical monographic series.

Surgical Practice of the Lahey Clinic. By Frank H. Lahey. Ed. 1. Pp. 897, with 376 illustrations. Philadelphia, 1941, W. B. Saunders Company.

This monograph is constituted essentially by a series of papers published previously, the majority of which appeared in 1939 or 1940; some, however, were published as long ago as 1937 and 1938. Dr. Lahey's interest in the standardization of tech-

Bruce Gill, Philadelphia, presented an end-result study, over a long period of years, of cases of congenital dislocation of the hip treated by him. This review is too valuable to be summarized; it should be carefully studied by everyone interested in this condition.

Carl Badgley, Ann Arbor, gave a brief review of a number of cases of spontaneous fracture of the neck of the femur following radiation for pelvic malignancy. He attributed most of these to the fractional method of treatment that was used in certain cases. It was interesting that most fractures united without difficulty but with some distortion and deformity unless they were nailed in proper position.

John Wilson and Francis McKeever, Los Angeles, reported a group of cases of osteomyelitis treated with sulfonamide drugs. The results were a distinct improvement over those of a former series of cases in which the drug was not used.

An unscheduled presentation was given by Donald R. Webster, Commander, Canadian Navy, on Immersion Foot. During the past year he has observed 142 victims who had been exposed in lifeboats or on rafts to cold water for a period of time varying from three days to three weeks. Prolonged immersion in cold water caused the feet to be cold, white, swollen, cyanotic in spots, numb, and lacking in tactile sensation. Rapid swelling, increased heat, and the appearance of blebs over the distal portion of the toes and sole of the foot resulted and was followed, in the severest cases, by gangrene. These patients were treated by refrigeration. When heat was used, gangrene with its tragic results developed. In the mild and moderately severe cases, within a period of from thirty to sixty days complete recovery was obtained by careful cleansing, application of ice bags over which insulating material was wrapped, and elevation of the extremity. The less severely injured patients suffered only some loss of tissue in one or more toes and the worst type of case required amputation.

J. A. Freiberg, Cincinnati, reported a series of approximately fifty cases of spinal fusion performed under a local anesthetic. He noted that this could be easily done, even in children. Some difficulty was encountered in obtaining grafts from the tibia because of pain arising from the endosteum. For this reason, a hole was drilled through the cortex into the marrow cavity at either end of the field from which the graft was to be taken. About 1 c.c. of procaine hydrochloride solution was then forced slowly into the marrow cavity at either end. Apparently, this sufficiently eliminated sensation from the endosteum to enable painless removal of the graft.

Fred M. Allen, New York (by invitation), presented a paper on Refrigeration Anesthesia for War Injuries of the Extremities. He reviewed the work that had been done at the City Hospital in New York in aged persons with diabetic and arteriosclerotic gangrene of the extremities. In these cases a tourniquet was applied at the proper level after the area had been desensitized by the application of ice bags. Morphine was administered, a tourniquet applied, and the extremity packed in ice up to and slightly above the level of the tourniquet. Amputation was then performed below the tourniquet, which was reapplied after the operation. Refrigeration of the extremity was continued for several days postoperatively during the healing period. It was gradually discontinued and the tourniquet finally removed. Excellent results were obtained. This technique was used in cases of compound fracture in which the vessels were so severely injured that amputation was necessary. It was proposed that ambulances and trains should be properly equipped with refrigerating units so that such injuries could be immediately frozen. This would enable transportation for an indefinite length of time without the risk of progress of infection or additional shock.

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THE FLOW OF LYMPH FROM BURNED TISSUE, WITH PARTICULAR REFERENCE TO THE EFFECTS OF FIBRIN FORMATION UPON LYMPH DRAINAGE AND COMPOSITION

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THE PROBLEM

IN A SERIES of papers summarized in 1938, Menkin¹ presented the idea that inflammatory processes differ in their tendency to spread, in relation to the local irritation they have caused. Inflammation has as its simplest elements, first, a great increase in capillary permeability, which floods the tissues with a slightly diluted blood plasma containing fibrinogen and prothrombin; second, a variable amount of tissue injury; and, third, migration of leucocytes. The last of these three features of inflammation is of little importance to the subject matter of this paper.

Menkin believed that lymphatic blockage by thrombosis and the conversion of the extravascular milieu into a fibrinous clot are of paramount importance in checking the spread of inflammation. The formation of fibrin lymphatically and extravascularly is due to the free escape of fibrinogen and prothrombin from the blood capillaries and the release of thromboplastic substances from injured cells. Menkin,² 1935, summed up the issues involved as follows: "Powerfully necrotizing irritants produce as a result of an increase in capillary permeability and of lymphatic damage, an extremely prompt reaction, perhaps best termed *fixation*. By this process, the area of injury is mechanically circumscribed and the dissemination of the irritant is prevented. *Staphylococcus aureus* is an example of such a bacterial irritant."³ Aleuronat

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unique in the performance of certain operations is so well known that this volume is bound to attract the surgeon interested in thyroid, biliary, gastric, or colonic surgery. In addition, there are excellent articles reprinted on certain aspects of thoracic, gynecologic, urologic, orthopedic and neurologic surgery and anesthesia.

The volume can be recommended as representing the practices of one of the strong surgical clinics in America. Some of the papers on the colon, in the light of present practices in other surgical clinics, have more historic than current interest. One of the chief defects of such a volume is that it is incomplete, that is, many procedures of interest to the general surgeon are missing. For instance, there are no papers on appendicitis, the pancreas, the spleen, and other subjects of interest to the abdominal surgeon; these defects are even more apparent in other provinces of the general surgeon.

Pediatric Gynecology. By Goodrich C. Schauffler. Pp. 384, with 66 illustrations. Chicago, 1942, The Year Book Publishers, Inc. \$5.

This unique book is the first of its kind and should be heralded by all who see the immature female for she belongs to a class of cases that often prove troublesome, with special and tactful approach being of prime importance. It presents more than gynecologic diseases but the selected abdominal surgical, urologic and proctologic diseases which must be considered in a differential diagnosis are correctly included. The medicolegal implications in sex crimes are presented and sound advice offered in a field with which the average physician is not conversant.

Much of the material included in this book has never before been published or has been widely scattered in brief communications on very narrow aspects of the subject. Few physicians ever have an opportunity to see and treat as many cases of this kind as has the author. Embryology and development of the female genitalia have been previously and adequately determined but the clinical phases are here thoroughly treated for the first time. Much of the material must be made up of the author's experience.

Worthy of particular mention are the author's recommendations for completeness in examination and exactness in bacteriologic diagnosis. Many practical procedures are given for gentleness in examination and treatment in order to obtain the cooperation of these young and easily alarmed patients. Detailed bacteriologic techniques are given, allowing the physician to proceed without further reference to other texts. Specific prescriptions are given for most infections.

The author's use of the popular but inaccurate and unscientific term "menometrorrhagia" must be condemned. Likewise, the designation of estrogenic or nonovulatory bleeding as menstruation is unfortunate. It must be pointed out that "to facilitate diagnosis" in cases with menorrhagia "curetting should be performed" not "immediately preceding an expected menstruation" but during the episode of uterine bleeding and after it has continued for at least four days. Unless this diagnostic procedure is adopted, all phases of irregular shedding of the endometrium will be missed and they should be common causes of menorrhagia at the menarche.

minutes. A burn so produced was severe. The overlying skin was porky and blanched except at the margin of the burn, where dilated, congested vessels were noted. Between the toes blisters formed in every case. The advantages of this procedure are: (1) It is susceptible to precise repetition from animal to animal, and in the different feet of the same animal. (2) Swelling is prompt and localized, and lymph can be collected from lymphatics immediately above the margin of the burn. (3) No break in the skin occurs for a number of hours, so that there is no external loss of fluid from the burn and no destruction of tissue not due to the burn itself. If burned tissue is a source of toxic substances, there is a maximal opportunity for their absorption. (4) It is easily possible to decrease and increase the amount of fibrin formation in the burned area, in the first case by intravenous heparin injections, and in the second case by subcutaneous infiltration of tissue extract immediately after dipping the foot in hot water and before swelling begins.

Examinations of Lymph.—It is a simple matter to cannulate lymphatics above the ankle joint in the hind legs and above the radiocarpal joint in the fore legs. If necessary, one can readily find vessels at higher levels, that is in the groin or at the base of the neck. Control specimens of lymph were obtained by gentle massage of the foot. After burning, lymph flowed spontaneously and in large amounts.

During prolonged collections of lymph, coagulation in the cannula was prevented by means of a wire with a small loop at the end, which could be inserted into the cannula to the neck. From time to time the loop was dipped in dry heparin, which dissolved in the lymph as it entered the cannula and steadily checked the annoyance of clotting. Lymph flow was measured volumetrically. Protein was determined refractometrically. Cell counts and changes in the color of the lymph were recorded as required, during experiments which lasted from 14 to 24 hours.

THE EXPERIMENTS

Immediately following the burn there was a spontaneous flow of lymph which increased rapidly over the first 3 to 6 hours and then diminished gradually during the next 20 hours. The protein percentage likewise increased sharply and this increase was maintained until the end of the experiment. Tissue fluid protein, when quantitated, was approximately the same as the lymph protein. This fluid was obtained by puncture of the burned and swollen part with a small needle. A short time after the puncture is made the fluid collected is grossly similar to the lymph, a clear fluid, tinged with hemoglobin and clotting quickly unless heparinized.

Fig. 1 shows the result of dipping the right front foot of a dog in boiling water for two minutes with the resulting lymph flow. The opposite foot was dipped in exactly the same way, but immediately after being removed from the hot water it was infiltrated subcutaneously with

is a chemical irritant of similar potency. Mild irritants, on the other hand, produce only a delayed reaction, thus allowing relatively free penetration of the irritant into the circulation for a considerable interval of time. Occlusion of the draining lymphatics in such instances often takes place as late as two days subsequently to the inoculation of the irritant. Hemolytic streptococci exemplify this type of irritant."

These very fundamental conceptions rest upon persistent and arresting experimentation carried on over many years. The point to be borne in mind is not that inflammation is of itself circumscribed, but that the destructive character of the inflammatory agent is extremely important in the localizing process. The more nearly invading organism and host are compatible, the more readily the invader spreads. If, however, the irritant causes cell destruction and outpouring of plasma from blood capillaries, then extravascular coagulation begins at once and the whole extravascular environment becomes a blood clot, which extends into the lymphatics. If blood capillaries are open through such regions, they will perform their functions of delivery and absorption of water and solutes. But lymph drainage with gradual spread of bacteria, viruses, or certain poisons will become negligible.

The relation of these generalizations to the problem of burns reached us through experiments by Field, Drinker, and White,⁴ 1932, who anesthetized dogs with nembutal, cannulated a lymphatic from a hind foot, and then immersed the foot in boiling water for two minutes, thus causing a very severe burn. Swelling began at once and there was an enormous outpouring of fluid from the blood capillaries which entered the lymphatics. Eventually a lymphatic end pressure developed which was that of the diastolic pressure of the blood. Lymph flowed freely from such a severely injured part during many hours.

There is an apparent disagreement between this last finding and the idea that the severity of injury and the restriction of lymph drainage correspond. Since burns have become a major problem in the present war and the issue of drainage from them of great moment, we have undertaken experiments to study lymph flow from tissues severely burned by surface sealding, the extent of lymphatic blockage and extravascular deposition of fibrin, and the possibility of shutting off lymphatic drainage by causing coagulation of all the fibrinogen escaping from the blood capillaries.

THE TECHNIQUE

In burns, the problem of selecting a standard procedure which can be applied comparatively to animal after animal is not so puzzling as in the case of surgical shock, but is of equal importance.

The Standard Burn.—After consideration, it was decided to use the simple method of Field, Drinker, and White,⁴ 1932, namely, dipping the foot of a dog, anesthetized with nembutal, into water at 100° C. for two

instantly, and during 12 hours was not resumed. Two other lymphatics from the region were cannulated during this time but no lymph could be collected.

Fig. 3 shows, above, the normal front feet of an anesthetized dog. The lower photograph is of the same feet 1 hour and 45 minutes after immersion in water at 100° C. for two minutes. Immediately after burning, foot *R* was injected subcutaneously with tissue extract; foot *L* was untreated in any way. It is clear enough that in foot *R*, where the exudate from the capillaries was caused to clot promptly and probably completely by the tissue extract injection, swelling is far more

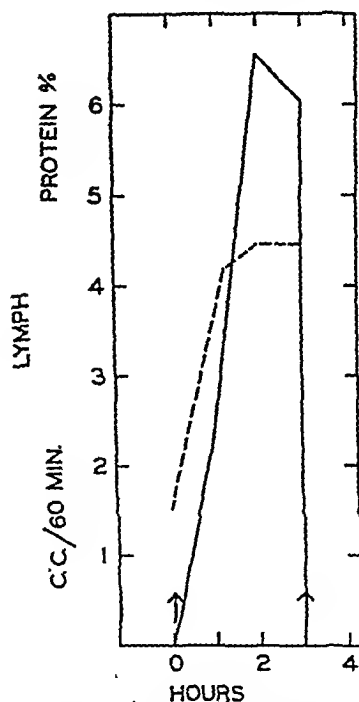


Fig. 2.—Three hours after 2 minutes' immersion of a front foot in water at 100° C., when swelling had become marked and lymph flow rapid, tissue extract was injected subcutaneously into the burned region. Lymph flow ceased instantly and was not resumed during the following 12 hours. Burn at 0, tissue extract injection at third hour. Solid line, lymph flow; broken line, percentage of protein in the lymph.

marked than in foot *L*, which was untreated and possessed unobstructed lymphatic drainage. A third pair of photographs (not used in this paper), taken 4 hours and 40 minutes after the burn, show foot *R* almost exactly as in Fig. 3. Foot *L* was more swollen but still behind the right foot, where coagulation of the exudate from the blood capillaries was assured by tissue extract injection.

It is clear that local swelling depends notably upon the degree to which coagulation of the exudate occurs with imprisonment of the water which leaks from the blood capillaries.

tissue extract made by grinding fresh beef lung, adding physiologic salt solution, and centrifuging to dispose of bits of tissue. Two things are obvious. First, there is an enormous increase in lymph flow from the right foot (1, Fig. 1) and the protein content (1, Fig. 1) of the lymph rises to more than 4 per cent and stays at that level. After some hours the lymph flow begins to fall, in all probability signalling a liberation of thromboplastic material at the site of the burn, which causes a sufficient degree of general coagulation to block lymph drainage.

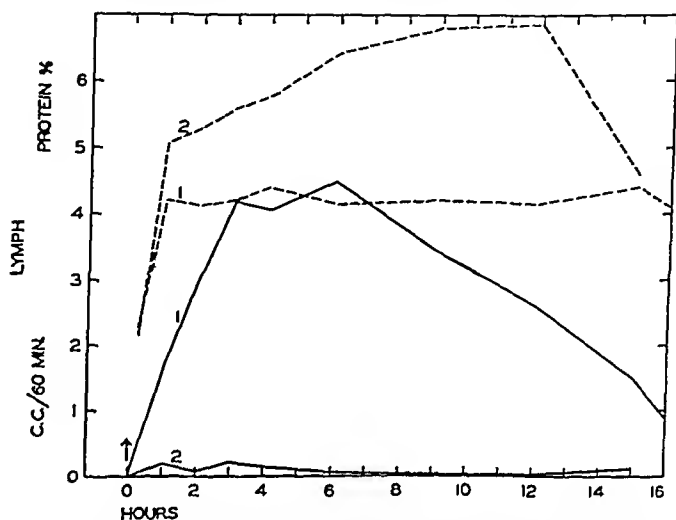


Fig. 1.—The effect on lymph flow and protein content of immersing the front feet of a dog in water at 100° C. for 2 minutes. Burn at the arrow O. Curves 1 and 1, for the right front foot, in the continuous line, show lymph flow in cubic centimeters per hour, and in the broken line the percentage of protein in the lymph during 16 hours following the burn. Curves 2 and 2 are similar in construction but in this case, immediately after a similar burn of the left front foot, tissue extract was injected subcutaneously. The foot swelled enormously, but lymph flow was negligible, and the small amount collected had a very high protein content. Ordinates, lymph flow in cubic centimeters per hour and protein percentage in lymph. Abscissae, time in hours.

In the case of the left front foot, dipped in boiling water and then infiltrated with tissue extract so that coagulation was maximal, it is obvious that lymph flow is negligible (2) and lymph protein high (2, Fig. 1). If one makes sections of the skin and subcutaneous tissues from feet treated in the manner described, it is easy to show extensive fibrin formation in the foot burned and injected with tissue extract. The opposite foot, burned, but given no extraneous supply of thromboplastic material, shows a meager amount of fibrin on section and it is obvious that coagulation has been insignificant.

Fig. 2 is one of a number of experiments in which a foot was dipped in water at 100° C. for two minutes with the usual prompt and extensive increase in lymph flow. At the end of the third hour, when lymph flow had become very rapid and swelling was extensive, the burned area was injected subcutaneously with tissue extract. Lymph flow stopped

experiment his blood and lymph were incoagulable. Immediately following heparinization the left foot was dipped in boiling water for 2 minutes and photographed as shown in Fig. 4. *L*, lower picture, exactly 2 hours later. Swelling has occurred but it is much less extensive than in the right foot, where a certain degree of coagulation of the exudate has occurred.

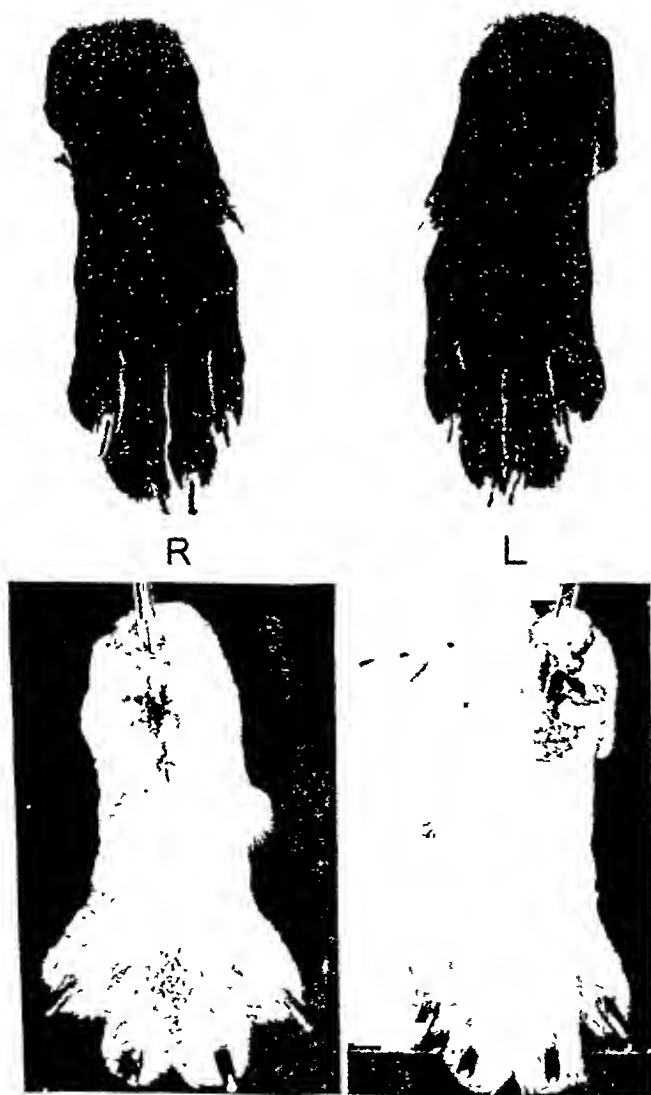


Fig. 4—The upper pair of front feet are normal. Prior to burning, a lymphatic had been cannulated in each case. The lower photograph of the right foot was taken 2 hours after 2 minutes' immersion in boiling water. The animal was then thoroughly heparinized and the left foot dipped in boiling water for 2 minutes. The lower photograph of the left foot shows much less swelling due to completed prevention of clotting by the heparin.

Fig. 4 illustrates an experiment in which the normal forefeet of a dog are shown above, and below, a photograph of the right foot 2 hours after 2 minutes' immersion in boiling water. No tissue extract was injected. Lymph flowed profusely from the cannula and clotted normally. At the end of 2 hours and after photographing the right foot, the dog was given a large dose of heparin intravenously so that for the rest of the

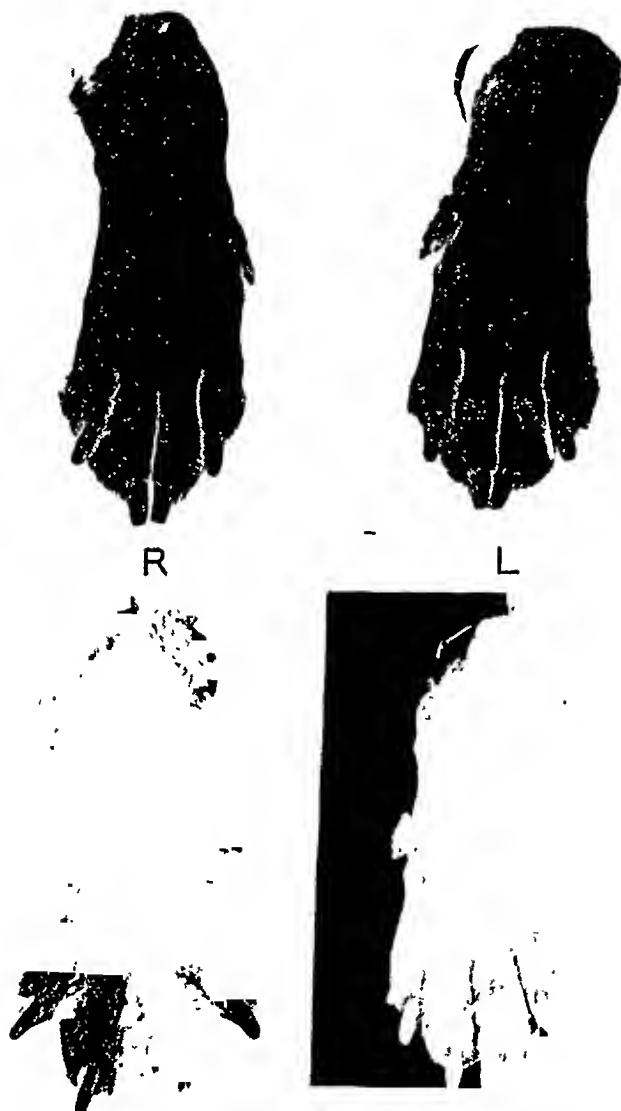


Fig. 3.—The upper pair of front feet are normal prior to simultaneous immersion in water at 100° C. for 2 minutes. In the lower photograph, foot *R* was injected subcutaneously with tissue extract immediately after burning, and foot *L* was allowed to take its normal course. Swelling in the foot *R*, which received tissue extract, is very marked as compared with foot *L*. The lower photograph was made 1 hour and 45 minutes after the burn.

foot are similarly stained. Heat alone, applied to a normally circulated part, does not induce generalized vascular thrombosis. There is, however, in burns so extensive as we have used, a certain amount of local hemolysis reflected within several minutes by pink coloration of the lymph collected from the foot. It is also possible to show that in addition to the direct local effect of heat in causing hemolysis, a hemolytic substance is liberated from the burned tissues which causes hemolysis in the dog and in vitro if lymph is collected and mixed with dog cells.

The experiments described in this paper are designed to establish the necessity for a standard, repetitive method of causing burns; to show that coagulation of the exudate from a burned area is capable of checking lymph flow, if it is complete enough; and to establish a basis for other experiments upon burns, such as the toxic nature of the lymph collected from burned areas, the effects of severe burns on capillary permeability in sound parts of the body, and the effect of confining the burned part in plaster of Paris immediately after removal from the boiling water and before swelling begins. Experiments in all these directions have been carried out and reports upon them will be issued as rapidly as possible.

SUMMARY

A simple method for making a standard burn by immersion of the foot of an anesthetized dog in boiling water is described.

The effects of coagulation of the exudate caused by the burn are described.

The failure to prevent collapse and death by blocking lymph flow is mentioned and will be discussed further in future papers.

REFERENCES

1. Menkin, V.: The Role of Inflammation in Immunity, *Physiol. Rev.* 18: 366, 1938.
2. Menkin, V.: Inflammation and Bacterial Invasiveness, *Am. J. Med. Sc.* 190: 583, 1935.
3. Menkin, V.: Studies on Inflammation. IX. A Factor in the Mechanism of Invasiveness by Pyogenic Bacteria, *J. Exper. Med.* 57: 977, 1933.
4. Field, M. E., Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation, *J. Exper. Med.* 56: 363, 1932.

DISCUSSION

These findings are of practical importance in several ways. First of all, lymphatic drainage can be blocked almost instantly and completely if the region damaged is either supplied with tissue extract artificially, or through the nature of the accident, so crushed and mutilated as to supply tissue extract naturally and thus bring about immediate coagulation of the exudate or blood from the capillaries. There is no doubt that localization of a spreading irritant, such as is faced in the growth of bacteria in an area of infection, may be beneficial. In the case of a burn of great severity, such as that used in these experiments, the heat acts for a given time and then the immediate problem for the animal consists in getting rid of the damage and its consequences. No one who sees the swelling and accumulation of coagulum, which occur locally when a foot is burned, as we have done, can fail to realize that if such an injury is to heal the animal must not only dispose of the tissue killed by the burn but must also get rid of a very large amount of clotted blood which is an unfortunate accessory to the injury. In an uninfected burn local accumulation of exudate, which is promoted greatly by fibrin formation, adds to the problem of healing though at the same time limiting absorption through the lymphatics. This last fact is not so important in connection with burns as we had hoped, since we have been able to show that if all four feet are burned for 2 minutes by immersion in boiling water, and prior to the burn the thoracic and right lymphatic ducts are cannulated so that no lymph enters the blood, the animal may die with the usual syndrome accompanying severe burns, lowered plasma volume, and falling blood pressure. It seems probable that a toxin is absorbed directly into the blood from burned areas and while the same substance is present in the lymph from such regions, blood absorption is so constant and so great as to cause death even though lymphatic participation in the disaster is excluded.

It is an interesting fact that though a severe burn such as has been used in these experiments must kill many cells in the skin and even in the deeper tissues of the foot, the burn does not cause immediate liberation of thromboplastic material in significant amounts, and it is only after 8 to 10 hours that lymph flow begins to slow down indicating, perhaps, that enough cell breakdown has occurred to convert prothrombin to thrombin and bring about extensive coagulation.

Another fact surprising to us consisted in the persistence of circulation through the capillaries of the burned foot, circulation which must be quite extensive. The foot swells rapidly when removed from the boiling water and lymph flows freely from cannulated vessels. These facts mean circulation through hyperpermeable capillaries and this fact is borne out if the animal is given a dye such as T-1824 intravenously. The lymph at once becomes blue and at autopsy the swollen tissues of the

Thus, in a patient in whom there was a tendency toward pulmonary edema from left heart failure, the intravenous administration of plasma on two occasions produced the signs and symptoms of acute pulmonary edema.

The following experiments are concerned with the effects of plasma infusions in animals in which the functioning pulmonary tissue has been acutely reduced. As in our earlier work, the experiments are divided into three groups. In the first group, a plasma infusion of 15 c.c. per kilogram of body weight was administered over a period of thirty minutes to normal cats. In the second group, approximately 71 per cent of the pulmonary tissue was surgically removed and the cats were observed for several hours afterward. In the third group of animals the same amount of pulmonary tissue was removed as in Group 2, and this procedure was followed by plasma infusions similar to those given the cats in Group 1.

METHOD

Cats were anesthetized by an intraperitoneal injection of a 5 per cent solution of sodium amytal (50 mg. per kilogram of body weight). A large glass cannula was tied into the opened trachea in the neck to ensure a free passage of air. The right femoral vessels were exposed and arterial blood samples were withdrawn from the femoral artery into an oiled syringe at the start of each experiment and at appropriate intervals thereafter. One cubic centimeter of this blood was placed in a small test tube containing 0.1 c.c. of solution of ammonium oxalate (1.2 per cent) and potassium oxalate (0.8 per cent) to prevent coagulation. The blood was allowed to stand for one-half hour in a Wintrobe hematocrit tube and was then centrifuged at 2000 r.p.m. for thirty minutes. The percentage of red cells was noted, the supernatant plasma was drawn off and the plasma protein concentration determined by the method of Barbour and Hamilton¹ as modified by Drew, Scudder, and Papps.³ The remainder of the blood in some experiments was transferred to an oxalated tube under oil and surrounded by ice. In these experiments carbon dioxide and oxygen content and oxygen capacity of the blood were determined by the Van Slyke manometric method.

Every sample of blood that was withdrawn was replaced with an equal quantity of blood obtained from another cat and injected into the femoral vein. The blood used for the replacement of samples was obtained under sterile conditions and kept in a sterile flask in the icebox until used. The blood was never more than seven days old. The plasma used for the infusions was obtained by bleeding a cat to death under sterile precautions. The blood was collected in sterile 50 c.c. tubes and centrifuged at 2000 r.p.m. for twenty minutes. The plasma was aspirated and stored in sterile flasks at 5° C. until used. Cultures of the plasma were not made before use in experiments, but any plasma emolysis or cloudiness was discarded.

EXPERIMENTAL PULMONARY EDEMA FOLLOWING LOBECTOMY AND PLASMA INFUSION

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IN A previous article⁴ it was demonstrated experimentally that when there has been an acute reduction in pulmonary tissue, a blood transfusion of a size well tolerated by normal animals may produce pulmonary edema, decreased saturation of the arterial blood with oxygen, and death. We also reported the histories of two patients who died some hours after the completion of bilateral lobectomies. Both patients received not only blood transfusions, but also rather large plasma infusions. In the two clinical cases reported it is conceivable that the infusion of plasma may have contributed to the pulmonary edema from which the patients died.

That pulmonary edema may occur during the course of a plasma infusion, when the heart is damaged and a tendency toward pulmonary vascular congestion is present, is illustrated by the following report.

CASE REPORT.—J. I., a 71-year-old white woman, entered the hospital complaining of marked shortness of breath. She had the signs and symptoms of congestive heart failure: an enlarged, tender liver and râles at the bases of both lungs. There was also a palpable enlargement of the thyroid gland. The basal metabolic rate was 53 per cent above normal. With rest in bed and digitalis the signs of congestive failure disappeared with the exception of the persistence of râles at the bases of both lungs. The basal metabolic rate fell to plus 40 and remained at that level.

After ten days of iodine medication a subtotal thyroidectomy was performed under local anesthesia. Following the operation the patient had several attacks of dyspnea associated with congestion at the bases of the lungs and signs of consolidation in the right lower lobe. X-ray confirmed the clinical diagnosis of bronchopneumonia of the right lower lobe. There was little febrile reaction, however, and under sulfathiazole and oxygen therapy the signs of pneumonia cleared up in three or four days, and thereafter her convalescence was relatively uneventful. On the eighth postoperative day she was given a plasma infusion because of a low plasma protein concentration. The infusion was given slowly but had to be discontinued after the administration of 300 c.c., because of marked dyspnea associated with loud moist râles throughout both lung fields.

A similar episode occurred on the tenth postoperative day. A plasma infusion was again administered cautiously but had to be discontinued because of the same symptoms of pulmonary edema as had appeared before. An hour or so after terminating the plasma infusion, the signs of pulmonary edema had completely disappeared and the patient was comfortable. On the evening of the same day the patient complained of pain in her chest, developed symptoms of shock, and died suddenly, presumably from a coronary thrombosis. Permission for autopsy was not granted.

dividing the vessels and bronchi of each lobe close to the pulmonary tissue. The presence or absence of froth in the trachea or bronchi was noted. The heart was removed from the pericardium, all the great vessels being divided close to the base of the heart. The resected pulmonary lobes and the heart were then weighed to an accuracy of 10 mg.

RESULTS

In general, the results were similar to those previously reported with blood transfusion.⁴ The mortality in the three groups of experiments is shown in Table I. The plasma infusion in normal cats produced no noticeable effects and none of the animals died, Table I, Group 1. Following the completion of the infusion, the animals were observed for periods of time varying from 3 hours and 30 minutes to 5 hours and 20 minutes, with two exceptions in which the animals were sacrificed 28 minutes and 2 hours and 20 minutes after the infusion. All these cats, without exception, were in good condition at the time of sacrifice.

In fifteen cats the right middle and all the lower lobes were resected as described above. Three cats in this group died, Table I, Group 2. Two of these had gross evidence of pulmonary edema: progressive cyanosis, coarse râles in the trachea, and froth exuding from the tracheal cannula. They died 1 hour and 5 minutes, and 1 hour and 10 minutes after completion of the lobectomy. The third animal died suddenly of cardiac arrest, presumably from ventricular fibrillation, 37 minutes after lobectomy during the injection of 10 c.c. of blood into the femoral vein to replace a blood sample which had been withdrawn a short time

TABLE I

MORTALITY FOLLOWING (1) PLASMA INFUSION IN NORMAL CATS, (2) REMOVAL OF ALL LOWER LOBES AND RIGHT MIDDLE LOBE AND (3) REMOVAL OF ALL LOWER AND RIGHT MIDDLE LOBES FOLLOWED BY PLASMA INFUSION

GROUP	TYPE OF EXPERIMENT	NUMBER OF ANIMALS	MORTALITY	
			NUMBER	PER CENT
1	Plasma infusion in normal cats	9	0	0
2	Resection of 71% of pulmonary tissue	15	3	20
3	Resection of 71% of pulmonary tissue followed by plasma infusion	11	8	73

before. This was the only instance in the thirty-five experiments reported here in which this accident occurred. The other twelve animals were observed for from 3 to 6 hours after the lobectomies and then sacrificed, with one exception when the animal was sacrificed 2 hours and 13 minutes after the lobectomy. None of these twelve cats were cyanotic, no tracheal râles were heard, and there was no fluid in the trachea at the time of sacrifice.

The control plasma infusions in Group 1 were in the majority of experiments made with the same lot of plasma which had been used in the experiments in Group 3. Thus, an experiment of the Group 3 type, with lobectomy followed by a plasma infusion, was followed the next day by a control experiment in which the same plasma was infused into a normal cat. The plasma infusions consisted of 15 c.c. plasma per kilogram of body weight, given over a period of thirty minutes in both the control Group 1 and the lobectomized animals, Group 3. The plasma was administered through a burette connected by rubber tubing to a glass cannula tied in the femoral vein.

In cats the right middle and all the lower lobes of the lungs comprise approximately 71 per cent of the pulmonary tissue. This figure was derived by determining the proportion of the weights of these lobes to the total lung weight in twenty-six normal cats. The figures varied between 66 and 75 per cent, averaging 71 per cent. The removal of the right middle and all the lower lobes was performed in Groups 2 and 3 by the same technique as previously employed.⁴ A No. 12 French catheter with an open end was threaded into the glass tracheal cannula until its tip lay within the trachea. While the pleural cavities were open, artificial respiration was administered by the intermittent insufflation of air through this catheter. Lobectomies were performed through an incision in the sixth intercostal space on either side. After division of the pulmonary ligaments, the hilar structures of the lobes to be removed were tied with a single ligature of heavy silk and the lobes were then resected. A small rubber tube with several perforations near the tip was introduced into each pleural cavity through a stab wound in the eighth intercostal space. The incision in the sixth interspace was then closed with a continuous suture, approximating the sixth and seventh ribs. The overlying muscles and skin were similarly sutured. At the conclusion of the bilateral operation, which required approximately twenty-five minutes to perform, the catheters draining the pleural cavities were connected to a constant source of 7 cm. water suction. A T tube inserted into the suction line was connected with a glass U-shaped water manometer in order to read respiratory variations in intrapleural pressure. After the chest was closed and suction established, artificial respiration was discontinued and the small rubber catheter withdrawn from the trachea. The lobes of the lungs removed at operation were kept in closed containers until their weights were determined.

At the conclusion of the experiment an autopsy was performed. Surviving animals were sacrificed by bleeding. The trachea was then clamped and the thoracic cavity widely opened by removing the sternum and the costal cartilages. Any fluid in the pleural cavities was noted and the amount measured. The color and condition of the lungs, or remaining lobes were noted. The lobes were resected separately by

of the vascular bed of these pulmonary lobes, as there was no gross evidence of fluid in the bronchi. The weights of the remaining lobes of the two cats in Group 2 which died with evidence of pulmonary edema fell within the range of the weights of the corresponding lobes of the eight animals in Group 3 which also died of pulmonary edema. Expressed as per cent of body weight they were 0.50 and 0.55; expressed as per cent of heart weight they were 114 and 144. The cat in Group 2 that died suddenly during the injection of blood had no evidence of pulmonary edema during life or at autopsy, and is included among the thirteen cats in Group 2 which were sacrificed and did not have pulmonary edema. The weight of the remaining lobes in this animal was 0.28 per cent of the body weight and 70 per cent of the heart weight.

The weights of the remaining lobes of the eight cats in Group 3 which died from pulmonary edema averaged more than three times the weight of the corresponding lobes in normal cats. They were grossly congested and edematous and froth poured from the openings of the cut bronchi. In the three cats in Group 3 which lived until sacrifice without evidence of pulmonary edema, the remaining lobes weighed approximately the same as those in the cats which had no pulmonary edema in Group 2. Expressed in per cent of body weight they were 0.22, 0.30, and 0.26; expressed in per cent of weight of heart they were 0.64, 0.69, and 0.80.

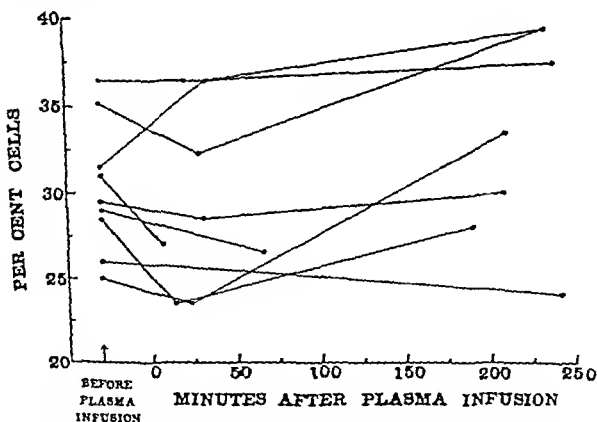


Fig. 1.—Hematocrit values in normal cats before and after plasma infusion.

The changes in hematocrit values and plasma protein concentrations are graphically shown in Figs. 1 to 6, inclusive. As can be seen, there are no consistent changes in these values except in Figs. 2 and 4. In Fig. 2 the hematocrit values before and after removal of 71 per cent of pulmonary tissue are shown. There is a definite tendency for the percentage of cells in the circulating blood to increase after the acute reduction in the pulmonary vascular bed. The explanation for this increase is not as yet clear. It is apparent that plasma was lost from the circulating blood, and one would expect this loss to occur through

In eleven cats the right middle and all the lower lobes were removed as in Group 2. From 25 minutes to 1 hour and 49 minutes after the completion of the lobectomies, the plasma infusion was started. Eight of the eleven cats died at intervals of time varying from 50 minutes to 2 hours and 15 minutes after the completion of the infusion, Table I, Group 3. Before death all these animals exhibited signs of pulmonary edema: râles in the trachea, marked cyanosis, and in most instances froth bubbling in the tracheal cannula. In three experiments the cats appeared to be unaffected by the plasma infusion. They were sacrificed at 2 hours and 5 minutes, 2 hours and 55 minutes, and 3 hours and 30 minutes after the completion of the plasma infusion, at which time there was no cyanosis, no tracheal râles could be heard, and there was no froth in the tracheal cannula. Thus, as can be seen in Table I, plasma infusion in normal cats carries no mortality, the resection of approximately 71 per cent of pulmonary tissue has a 20 per cent mortality, while the resection of 71 per cent of pulmonary tissue followed by a plasma infusion has a 73 per cent mortality.

The evidence for the presence of pulmonary edema in Groups 2 and 3 was the manner of death, with progressive cyanosis, labored respiration and froth in the trachea, and the autopsy findings. In all the animals that died from pulmonary edema, froth was present in the trachea and exuded from the main stem bronchi when cut. In Table II the weights

TABLE II

WEIGHT OF RIGHT UPPER AND LEFT UPPER AND MIDDLE LOBES EXPRESSED AS PER CENT OF WEIGHT OF BODY AND OF HEART IN FOUR GROUPS OF CATS*

GROUP	TYPE OF EXPERIMENT	PER CENT WEIGHT OF BODY		PER CENT WEIGHT OF HEART	
		VARIATION	AVERAGE	VARIATION	AVERAGE
	26 normal cats	.12 to .22	.16	33 to 57†	44†
1	9 normal cats with plasma infusion	.17 to .24	.20	43 to 60	51
2	Removal of right middle and all lower lobes in 13 cats	.20 to .35	.26	54 to 89	70
3	Removal of right middle and all lower lobes followed by plasma infusion in 8 cats	.43 to .91	.56	99 to 184	139

*In normal cats, in normal cats with plasma infusion, in cats from which the right middle and all lower lobes had been removed, and in cats with the same amount of pulmonary tissue removed, followed by a plasma infusion.

†Figures obtained in seven normal cats.

of the right upper and left upper and middle lobes, that is, the remaining lobes when lobectomy was performed, are expressed in relation to the weight of the body and of the heart in Groups 1, 2, and 3, and in normal cats. These lobes in normal cats given plasma infusions were slightly heavier than in normal cats without plasma infusion. In the thirteen cats in Group 2 which did not develop pulmonary edema, there was an increase in the weight of the remaining lobes of approximately 60 per cent. This increase in weight was probably due to congestion

of the vascular bed of these pulmonary lobes, as there was no gross evidence of fluid in the bronchi. The weights of the remaining lobes of the two cats in Group 2 which died with evidence of pulmonary edema fell within the range of the weights of the corresponding lobes of the eight animals in Group 3 which also died of pulmonary edema. Expressed as per cent of body weight they were 0.50 and 0.55; expressed as per cent of heart weight they were 114 and 144. The cat in Group 2 that died suddenly during the injection of blood had no evidence of pulmonary edema during life or at autopsy, and is included among the thirteen cats in Group 2 which were sacrificed and did not have pulmonary edema. The weight of the remaining lobes in this animal was 0.28 per cent of the body weight and 70 per cent of the heart weight.

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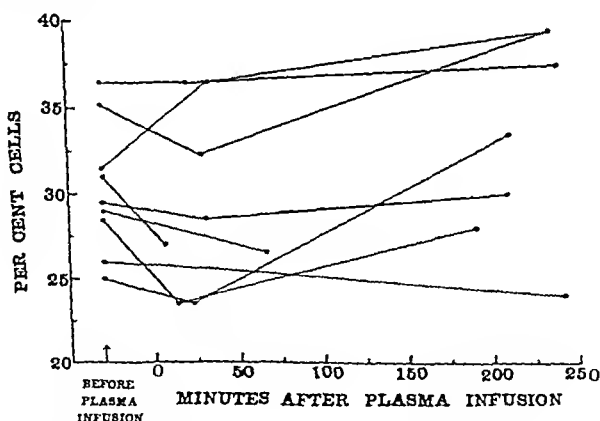


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The changes in hematocrit values and plasma protein concentrations are graphically shown in Figs. 1 to 6, inclusive. As can be seen, there are no consistent changes in these values except in Figs. 2 and 4. In Fig. 2 the hematocrit values before and after removal of 71 per cent of pulmonary tissue are shown. There is a definite tendency for the percentage of cells in the circulating blood to increase after the acute reduction in the pulmonary vascular bed. The explanation for this increase is not as yet clear. It is apparent that plasma was lost from the circulating blood, and one would expect this loss to occur through

the capillary and alveolar walls of the remaining pulmonary lobes because of the existing congestion. However, only two of the animals in this group developed pulmonary edema in amounts sufficient to be

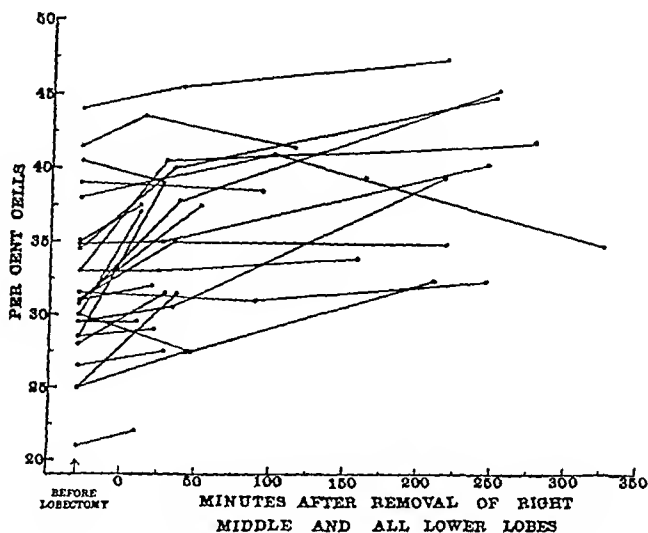


Fig. 2.—Hematocrit values before and after removal of the right middle and all lower lobes.

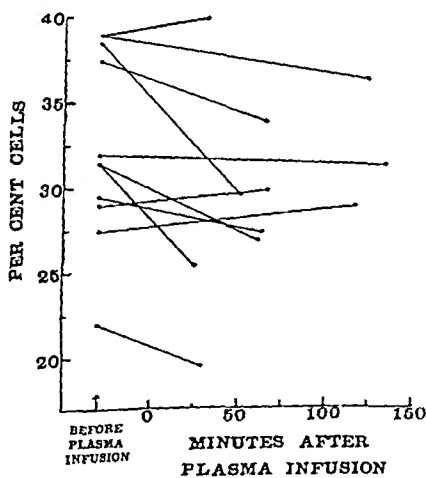


Fig. 3.—Hematocrit values before and after plasma infusion in lobectomized cats.

noticed grossly and to cause death. A similar hemoconcentration following extensive removal of pulmonary tissue was noted in the experiments previously reported.

In Fig. 4 there is shown a consistent increase in the plasma protein concentration in normal cats following a standard plasma infusion. The plasma protein concentration in animals of Group 2, as shown in

Fig. 5, shows variable changes which are too irregular to be significant. However, in Fig. 6 it can be seen that in only three experiments was there a significant rise in the plasma protein concentration following

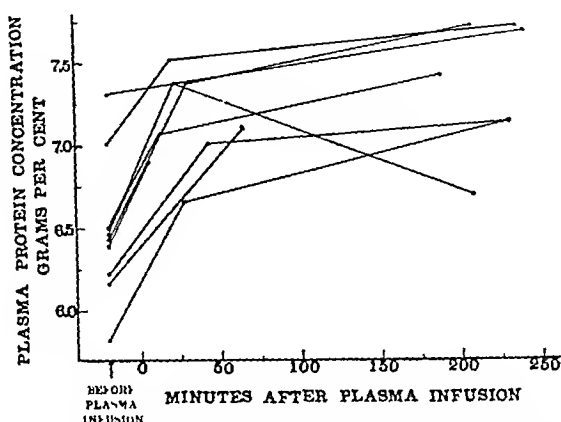


Fig. 4.—Plasma protein concentration in normal cats before and after plasma infusion.

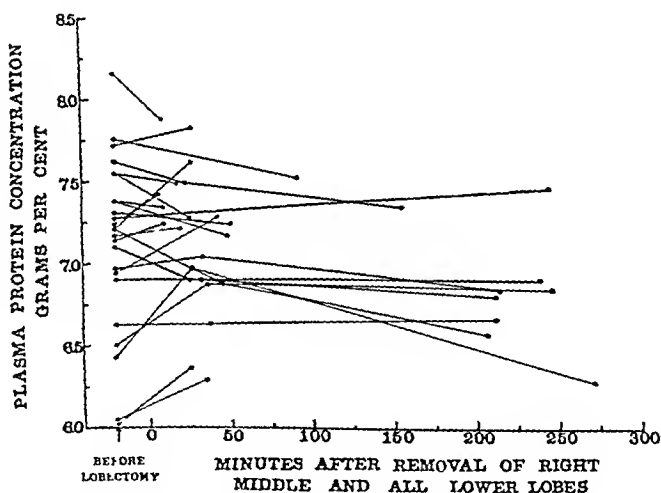


Fig. 5.—Plasma protein concentration before and after removal of the right middle and all lower lobes.

a plasma infusion in lobectomized cats. In the remaining eight experiments there was practically no change in concentration. When these results are compared with those shown in Fig. 4, it is apparent that protein was lost from the blood stream by the animals in Group 3. The pulmonary edema which followed the infusions of plasma undoubtedly represents some of this lost plasma.

The concentration of the protein in the plasma used for the infusions varied between 5.7 and 6.6 Gm. per cent, averaging 6.2 Gm. per cent, with one exception. In this instance the plasma used had a concentra-

tion of only 4.8 Gm. per cent, and this plasma was used for infusion in one of the three animals in Group 3 which survived the infusion following a lobectomy. This fact, however, is probably without significance, as the other two animals which survived in Group 3 were infused with plasma having a protein concentration of 6.0 and 6.6 Gm. per cent. In six instances fluid was obtained from the tracheae of animals dying with pulmonary edema for determinations of the protein concentration, which varied between 5.2 and 6.2 Gm. per cent, and averaged 5.7 Gm. per cent. The plasma protein concentration of the blood of thirty-three normal cats varied between 5.8 and 8.2 Gm. per cent, averaging 7.0 Gm. per cent. Thus it is evident that the fluid which filled the bronchi and tracheae of the animals dying from pulmonary edema consisted of only slightly diluted plasma.

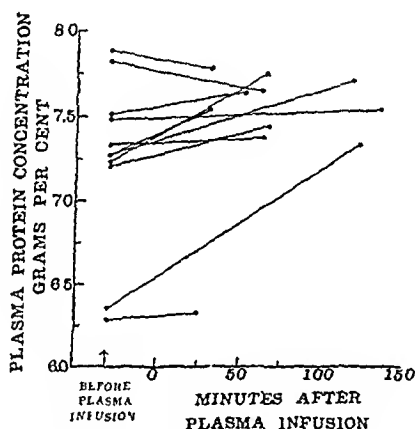


Fig. 6.—Plasma protein concentration before and after plasma infusion in lobectomized cats.

A few determinations were made of the saturation of the arterial blood with oxygen in the three groups of experiments. The results were entirely similar to those reported previously with blood transfusions following lobectomy. In Group 1, the saturation of the arterial blood with oxygen was determined in three instances following plasma infusions in normal cats. In each instance the blood was found to be adequately saturated with oxygen, the figures being 96, 93, and 95 per cent. In Group 2 the saturation of the arterial blood with oxygen was determined in six instances at time intervals after the completion of the lobectomy varying from 1 hour and 51 minutes, to 5 hours and 22 minutes. In each instance the blood was adequately saturated with oxygen, the values being 92, 92, 94, 93, 95, and 100 per cent saturation. In the two animals that died from pulmonary edema, the oxygen saturation was not determined. In the animal that died suddenly during the injection of blood, the arterial blood was 99 per cent saturated with oxygen 10 minutes before death. In Group 3, the saturation of arterial

blood with oxygen was determined in four experiments following the plasma infusion. In three of these experiments the animals died 21, 20, and 32 minutes after the blood sample was taken for analysis. The saturation of the arterial blood with oxygen was respectively 66, 58, and 73. In the fourth experiment the animal survived the plasma infusion and the arterial blood was 94 per cent saturated with oxygen 2 hours and 12 minutes after the completion of the infusion.

DISCUSSION

Edema occurs because of increased capillary blood pressure, decreased colloid osmotic pressure of the blood plasma, or because of increased permeability of the capillary endothelium. It is the first of these causes which we believe operates in the pulmonary edema consequent upon blood or plasma infusions following acute reduction of the pulmonary vascular bed. After removal of 71 per cent of pulmonary tissue, the entire output of the right heart must pass through the remaining 29 per cent of the pulmonary vascular bed. If the cardiac output is not diminished, the increase in blood flow through the left upper and middle and right upper lobes would amount approximately to 345 per cent. That there is no gross diminution of the cardiac output is evidenced by the fact that the systemic arterial and venous blood pressures are within normal limits following lobectomies.⁴ With exercise the blood flow through normal human lungs may be increased from 600 to 800 per cent² without the production of pulmonary edema, although under these circumstances there is an increased volume of blood in the lungs. In the experiments reported here the increase in weight of the remaining lobes following removal of 71 per cent of pulmonary tissue might be due to an increased volume of blood in the pulmonary vascular bed.

In conclusion, the frequent and ever-increasing use of plasma and blood transfusions in all fields of surgery justifies a word of caution as regards their indiscriminate use in thoracic surgery. When there has been any impairment of cardiorespiratory function, following or during a thoracic operation, it seems to be advisable to employ intravenous fluids which tend to remain in the blood stream, such as blood and plasma, with a certain degree of caution, and to be on the lookout for developing signs of pulmonary edema.

SUMMARY

1. A plasma infusion of 15 c.c. per kilogram of body weight was given at a constant rate over a period of thirty minutes to nine normal cats. There were no signs of pulmonary edema before sacrifice or at autopsy.
2. The right middle and all the lower lobes of the lungs were removed from fifteen cats. Two of these animals died from pulmonary edema and there was one accidental death. The other twelve were sacrificed

tion of only 4.8 Gm. per cent, and this plasma was used for infusion in one of the three animals in Group 3 which survived the infusion following a lobectomy. This fact, however, is probably without significance, as the other two animals which survived in Group 3 were infused with plasma having a protein concentration of 6.0 and 6.6 Gm. per cent. In six instances fluid was obtained from the tracheae of animals dying with pulmonary edema for determinations of the protein concentration, which varied between 5.2 and 6.2 Gm. per cent, and averaged 5.7 Gm. per cent. The plasma protein concentration of the blood of thirty-three normal cats varied between 5.8 and 8.2 Gm. per cent, averaging 7.0 Gm. per cent. Thus it is evident that the fluid which filled the bronchi and tracheae of the animals dying from pulmonary edema consisted of only slightly diluted plasma.

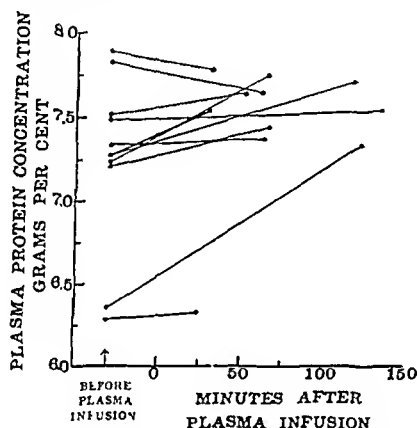


Fig. 6.—Plasma protein concentration before and after plasma infusion in lobectomized cats.

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THE RENAL RESPONSE TO HYPERTONIC SUCROSE SOLUTIONS*

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INTRAVENOUS hypertonic sucrose has been widely used in the clinic for a variety of purposes without apparent ill effect. Recently, however, the question has been raised as to whether such indiscriminate use is justified since it has been reported to lead to impairment of kidney function and to histologic evidence of tubular damage¹⁻⁷. Further, the changes found in the renal tubular epithelium might possibly affect the mechanism of nephrogenic hypertension. It is also conceivable that the increased load on the kidney resulting from the retention of waste products which sucrose injections cause, could result in an aggravation of the hypertension. These considerations led us to reinvestigate the action of hypertonic sucrose on normotensive and hypertensive dogs with and without pre-existing renal excretory insufficiency.

LITERATURE

The most extensive clinical use of sucrose is its employment in the reduction of intracranial pressure.^{8,12} Intravenous hypertonic sucrose lowers intracranial pressure without the secondary rise seen with the use of hypertonic dextrose.⁸ Other uses for sucrose have been recently suggested, also based for the most part on a similar tissue dehydrating action. It has been utilized preoperatively in glaucoma,¹³ in the treatment of chronic hypertension,¹⁰ as a diuretic agent in nephrosis¹⁴ and in other conditions,¹⁵ in chronic alcoholism,¹⁶ as well as in bronchial asthma in conjunction with adienahn.¹⁷ It has been utilized to measure glomerular clearance¹⁸ and extracellular fluid.¹⁹

The cardiovascular response to the hypertonic sucrose solution is a transient hypervolemia with attendant increases in venous pressure, heart rate, cardiac minute output, and arterial blood pressure.²⁰ These effects are transitory. Almost all the sucrose is excreted within the first few hours.¹⁸

It has been clearly demonstrated in dogs,^{1,3} in rabbits,² and in man,^{2,4-7} that intravenous injections of hypertonic sucrose in large amounts lead within an hour to swelling of the convoluted tubules of the kidney, associated with a fine vacuolar degeneration, nuclear shrinkage, and the presence of granular exudate in the glomerular lumen. These changes reach a maximum on the third day and then gradually subside. With repetition of the injections every third day or oftener, the renal changes are found to be more severe and the phenolsulfonphthalein clearance is markedly lowered.² Even after several sucrose injections the function and appearance of the renal epithelium show a remarkable ability to return to normal,^{2,3} but a prolonged series of injections tends to produce sclerosis and atrophy of the kidney with a reduction in renal excretory function.^{2,3} Dextrose,³ sorbitol,² and mulin²¹ apparently do not lead to such lesions.

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between 4 and 6 hours after the operation. None of these animals showed evidence of pulmonary edema before death or at autopsy.

3. In eleven animals after removing the same lobes of the lungs, a plasma infusion of 15 c.c. per kilogram of body weight was given over a period of 30 minutes. Three of these animals lived and were sacrificed between 2 and 4 hours later. There was no evidence of pulmonary edema before death or at autopsy. The remaining eight animals died from 1 to 2 hours after completion of the infusion with clinical evidence of pulmonary edema and gross evidence at autopsy of fluid filling the tracheae and bronchi.

4. The hematocrit values showed no constant change before and after plasma infusions in the normal and in lobectomized cats. There was generally a definite increase in the hematocrit values following the acute removal of 71 per cent of pulmonary tissue.

5. The plasma protein concentration was consistently elevated following plasma infusions in normal cats. There was a variable change in plasma protein concentration before and after lobectomy and after plasma infusion in the group of lobectomized cats.

6. The saturation of the arterial blood with oxygen was determined in a few experiments. The arterial blood was adequately saturated with oxygen in all the normal and lobectomized animals which did not die from pulmonary edema. In the animals dying from pulmonary edema, saturation of the arterial blood with oxygen was decreased.

7. There was no significant increase in the weights of the lungs of normal cats following plasma infusion. Following removal of the right middle and all the lower lobes in the animals that did not develop pulmonary edema, the remaining lobes showed an increase in weight of approximately 60 per cent. After removal of the lobes mentioned, followed by a plasma infusion, the animals that died showed an increase in the weight of the remaining lobes of approximately 300 per cent.

CONCLUSION

In cats, when there has been an acute reduction of pulmonary tissue, a plasma infusion of a size well tolerated by normal animals may produce death from pulmonary edema.

REFERENCES

1. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, *J. Biol. Chem.* 69: 625, 1926.
2. Best, C. H., and Taylor, N. B.: *Physiological Basis of Medical Practice*, Baltimore, 1937, William Wood & Co.
3. Drew, C. R., Scudder, J., and Papps, J.: Controlled Fluid Therapy with Hematocrit, Specific Gravity and Plasma Protein Determinations, *Surg., Gynec. & Obst.* 70: 859, 1940.
4. Gibbon, J. H., Jr., Gibbon, M. H., and Kraul, C. W.: Experimental Pulmonary Edema Following Lobectomy and Blood Transfusion, *J. Thoracic Surg.* 12: 60, 1942.

transient azotemia occurred. After an interval of a week, two dogs received another series of daily injections of 200 c.c. of sucrose for ten and thirteen days, respectively. This was accompanied by a transient rise in blood N.P.N. which returned to the normal level before the injections were ended. No significant changes in blood pressure were noted in this series.

3. *Tolerance to Sucrose.*—The recovery from the renal damage following the sucrose injections despite continuation of the injections suggested that a more adequate tolerance might be established by the use of graded doses. This possibility was tested in fifteen dogs, six normal and nine with hypertension and reduced renal reserve. These dogs were given daily sucrose injections beginning with 10 c.c. on the first day and with the amount injected increased by 20 c.c. each day, until 200 c.c. was reached; this was followed by six injections of 200 c.c. in the next six days. No evidence of renal impairment was noted either in the blood N.P.N. or in the ability to concentrate the urine on dehydration two days after the end of the injections. No alterations in blood pressure were observed.

Four other animals with reduced renal excretory reserve and hypertension were given daily injections of 10 c.c. of sucrose for four days, followed by daily injections of 200 c.c. of sucrose for four days. A transient increase in blood N.P.N. and a marked reduction in the ability to concentrate urine were observed. The blood N.P.N. quickly returned to the previous level, and after ten to twenty-five days the kidneys had almost completely regained their previous function and concentrating ability.

4. *Deaths Occurring During the Experiments.*—Eight of the animals receiving sucrose died during the period of injections, six during a period of hot weather. Death occurred from six to twenty-seven days after the injections were begun. In all, death was associated with pulmonary involvement; six died of pneumonia, and the other two dogs died with pulmonary edema and azotemia.

DISCUSSION

The injection of hypertonic sucrose has been reported to lead to anatomic changes particularly in the tubules.¹⁻⁷ It is clear that for a few days, at least, the renal excretory reserve is reduced. In animals in which an initial large amount of renal reserve was present, no demonstrable effects were noted in the blood N.P.N. level nor did protein or other abnormal formed elements appear in the urine. However, the ability of the kidney to concentrate urine was reduced, reflecting the renal tubular alterations. The absence of blood N.P.N. elevation may be due to the polyuria induced by the sucrose, which may become sufficiently large to clear the blood of nonprotein nitrogenous products

METHOD

Hypertonic solutions were prepared by dissolving 50 Gm. of sucrose* in distilled water and diluting to 100 c.c. Blood pressures were determined with the Hamilton manometer²² on trained unanesthetized dogs according to the technique used in this laboratory.²³ Hypertension was induced by the technique of Goldblatt,²⁴ and relative renal excretory insufficiency was either an associated circumstance in such animals or was induced by temporarily completely occluding the renal arteries for one hour.²⁵ Renal excretory impairment was evaluated by determining blood N.P.N.† and by comparing the specific gravity of the urine after dehydrating the animals for twenty-four hours during which time only dry food was permitted.

RESULTS

1. *Unoperated Normotensive Dogs Without Preliminary Evidence of Renal Excretory Insufficiency.*—Seven dogs received 200 c.c. of 50 per cent sucrose daily for five, six, six, nine, ten, ten, and thirteen consecutive days, respectively. In three of these animals a rise in blood N.P.N. to about 60 mg. per cent was evident on the third day of injections, but the N.P.N. returned to normal after three more days. The other four dogs showed no change in N.P.N. Before the series of injections the animals were able, after twenty-four hours without water, to concentrate the urine to a specific gravity of 1.050. Two days after the injections were completed the kidneys could concentrate only to about 1.025. However, a week later the control-concentrating ability was usually regained. The urine remained clear and free of albumin and casts. The blood pressure of all seven dogs remained unchanged during and after the injection period.

2. *Normotensive and Hypertensive Dogs With Preliminary Evidence of Reduced Renal Excretory Reserve.*—Two normotensive and three hypertensive dogs with reduced renal excretory reserve, due to partial occlusion of the renal arteries, were used in this series. Each dog received a total of 500 c.c. of 50 per cent sucrose administered in 100 c.c. doses every third day. No effect was observed on the blood N.P.N. level, but the renal concentrating power was definitely reduced in each case as in the preceding series. These animals then received daily injections of 100 c.c. of 50 per cent sucrose over eight days. During this period all showed a transient rise in blood N.P.N. with the appearance in the urine of formed elements and albumin, red and white blood cells. The ability of the kidney to concentrate urine remained at a low level, but rose to normal values a week after the cessation of injection.

After four weeks, all five dogs received daily injections of 200 c.c. of 50 per cent sucrose for seven, ten, twelve, thirteen, and sixteen days respectively. This procedure led to a rise in blood N.P.N., pulmonary edema, azotemia, and death in two animals. In the other three dogs a

*We are grateful to Dr. M. Gordon of Endo Products for supplying us with the ampoules of 50 per cent sucrose.

†We are indebted to Dr. D. J. Cohn, Head of the Department of Biochemistry, for these determinations.

SUMMARY

1. Large amounts of hypertonic sucrose given intravenously to normal dogs led to a transient reduction in the ability of the kidney to concentrate urine, without elevation in blood N.P.N.

2. In dogs with reduced renal excretory reserve treated as above, the reduction in concentrating capacity was associated with a transient rise of blood N.P.N. Adjustment to the daily injections was indicated by the return of the N.P.N. to normal even though the injections were continued.

3. A relative tolerance to sucrose was demonstrated by the use of gradually increasing daily injections.

4. Blood pressure remained unchanged in both normotensive and hypertensive dogs, with and without previous renal involvement.

5. The use of hypertonic sucrose requires caution in cases with renal or myocardial involvement, in general infections or in dehydrated states.

ADDENDUM

Since this paper was written, Rigdon and Cardwell²⁹ reported nine more cases with anatomic renal involvement following hypertonic sucrose. They found that the renal response depended in part upon the state of dehydration of the patient.

REFERENCES

1. Lamy, H., Mayer, A., and Rathery, F.: *Études sur la diurèse. III. Modifications du rein au cours de l'élimination de l'eau et des crystalloïdes*, J. de physiol. et de path. gen. 8: 624, 1906.
2. Helmholtz, H. F.: Renal Changes in the Rabbit Resulting From Intravenous Injection of Hypertonic Solution of Sucrose, J. Pediat. 3: 144, 1933.
3. Lindberg, H. A., Wald, M. H., and Barker, M. H.: Renal Changes Following Administration of Hypertonic Solution (50 per cent sucrose, 50 per cent d. sorbitol, 50 per cent dextrose), Arch. Int. Med. 63: 907, 1939.
4. Cutler, H. H.: Effect of Sucrose on the Kidney, Proc. Staff Meet., Mayo Clin. 14: 318, 1939.
5. Klemperer, P.: Effects of Intravenously Injected Sucrose on the Kidney, Arch. Path. 27: 946, 1939.
6. Anderson, W. A. D., and Bethea, W. R.: Renal Lesions Following Administration of Hypertonic Solutions of Sucrose; Report of Six Cases, J. A. M. A. 114: 1983, 1940.
7. Anderson, W. A. D.: Sucrose Nephrosis and Other Types of Renal Tubular Injuries, South. M. J. 34: 257, 1941.
8. Bullock, L. T., Gregerson, M. L., and Kinney, L.: The Use of Hypertonic Sucrose Solution Intravenously to Reduce Cerebrospinal Fluid Pressure Without a Secondary Rise, Am. J. Physiol. 112: 82, 1935.
9. Masserman, J. H.: Effect of Intravenous Administration of Hypertonic Solutions of Sucrose With Special Reference to the Cerebrospinal Fluid, Bull. Johns Hopkins Hosp. 57: 12, 1935.
10. Murphy, F. D., Hershsberg, R. A., and Katz, A. M.: The Effect of Intravenous Injection of Sucrose Solutions (50 per cent) on the Cerebrospinal Fluid Pressure in Cases of Chronic Hypertension, Am. J. M. Sc. 192: 510, 1936.
11. Jackson, H., Dickerson, D., and Gunther, A.: The Reduction of Intracranial Pressure in Cerebral Injury by the Intravenous Use of Hypertonic Sucrose Solution, Am. J. Surg. 106: 161, 1937.
12. Hahn, E. V., Ramsey, F. B., and Kohlstadt, K. G.: Clinical Experience in the Use of Sucrose Instead of Dextrose in the Osmotic Therapy of Increased Intracranial Pressure Occurring in Cases of Acute Brain Injury, J. A. M. A. 108: 773, 1937.
13. Dyar, E. W., and Matthew, W. B.: Use of Sucrose Preparatory to Surgical Treatment of Glaucoma, Arch. Ophth. 18: 57, 1937.

even when the excretory ability of the kidneys is reduced. On the other hand, in animals with pre-existing reduced excretory capacity the introduction of the hypertonic sucrose may lead to a transient relative renal excretory insufficiency as evidenced by a rise in blood N.P.N. as well as by a notable reduction in ability to concentrate urine.

The recovery of the ability of the kidney to cope with the systemic excretory needs even while the sucrose injections were being continued suggests that the kidney can in some way compensate for the new conditions. The mechanism of this adjustment is at present not understood. It is significant, however, that gradually increasing dosages of sucrose may avoid even the temporary renal excretory insufficiency. This compensatory mechanism apparently requires gradual rather than abrupt increase in the sucrose doses. Further, the compensation to sucrose injections is quickly lost since, after a short period of rest, a new series of injections will again lead to transient renal excretory insufficiency.

The absence of blood pressure changes in either normotensive or hypertensive dogs is evidence that the changes induced in the renal parenchyma by the hypertonic sucrose do not initiate or inhibit the hypertensive mechanism. During the period of relative retention of excretory products the absence of a rise in the blood pressure once again suggests that the renal factors responsible for the initiation of hypertension and those having to do with the failure of the kidney to excrete waste products are discrete.²⁷ The mechanism involved in nephrogenic hypertension is, thus, not dependent on the disordered state of tubular metabolism seen in our animals but probably occurs in some other region of the renal apparatus.

Since the tissues of man contain no invertase,²⁶ injected sucrose may become available for use by pathogenic organisms and may possibly lead to increased virulence of infections, particularly in dehydrated states, which are aggravated by the injection of hypertonic sucrose.

In our experiments extreme conditions were induced by the injection of large amounts of hypertonic sucrose. This was done to determine, if possible, the maximal ability of the normal and abnormal renal apparatus to adjust to these conditions. Except for the preliminary damage brought on by the hypertonic sucrose, little permanent damage was done. It has also been shown that the cardiac minute output is greatly increased after hypertonic sucrose as a result of an increased plasma volume and venous pressure.²⁸ Evidently a strain is placed upon the heart as well as upon the kidneys. However, it would appear that in the absence of myocardial and renal damage, injections of moderate amounts of hypertonic sucrose are not contraindicated. This agrees with the clinical experience that no deaths have been attributed directly to hypertonic sucrose injections, during the long history of its use for various purposes.

ANEURYSM OF THE TEMPORAL ARTERY

A SPONTANEOUS CASE CURED BY OPERATION

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THE history of treatment of peripheral aneurysms dates back to antiquity. In the third century Antyllus used double ligature incision, and packing. In the fourth century Philagrius advocated excision. In the eighteenth century Hunter demonstrated the value, in certain cases, of ligation at a distance, proximal to arterial branches. The advisability of this procedure obviously depends upon the regional anatomy and the degree of enlargement of the anastomotic channels. The danger of circulatory deficiency and gangrene, which is of paramount importance in the management of many peripheral aneurysms, is of no significance in the temporal region because of the rich anastomoses of the branches of the external carotid artery. In 1884 and 1885, De Santi made a special study of temporal aneurysms and reviewed thirty-seven cases, three of which were considered spontaneous true aneurysms. His record of Thomas Bartholin's case, which was recorded in 1740, is an interesting example of the traumatic type. The following is a translation of De Santi's account.

The oldest observation of aneurysm of the temporal artery is that of Thomas Bartholin. He was called to a child of seven years, whose mother had struck him a violent blow with a stick on the left side of his head.

"It produced instantly," he said, "a pulsatile tumor about the size of a tangerine, blackish, disappearing upon pressure, which in eight days enlarged finally to cover half of the head, i.e., the temple and the forehead from the sagittal suture to the eye. The consulted doctors, being convinced that a dangerous remedy was preferable to certain death, and having obtained the consent of the mother, opened the tumor with a bistouri. It made a notable hemorrhage, but the blood which spurted was arrested by astringents and after some days this child recovered by the grace of God and was returned to his sorrowful mother."

An excellent comprehensive review of the subject of temporal aneurysm was published by Winslow and Edwards in 1934 and 1935. They tabulated the important data on cases from the literature: 9 spontaneous, 79 traumatic, 5 unclassified, 15 arteriovenous, and 10

14. Lowenburg, H., Sr., and Nensen, S.: Intravenous Injection of 50 per cent Solution of Sucrose in Edema, *Arch. Pediat.* 53: 762, 1936.
15. Strohm, J. G., and Osgood, S. B.: Intravenous Sucrose as a Diuretic, *Northwest Med.* 35: 89, 1936.
16. Hilton, J. P., and Anderson, D. M.: Sucrose Solution in the Treatment of Alcoholism and Confusional States, *Rocky Mountain M. J.* 35: 227, 1938.
17. Keeney, L. L.: The Effectiveness of Intravenous Hypertonic Sucrose and Adrenalin in the Treatment of Status Asthmaticus, *J. Allergy* 9: 497, 1938.
18. Keith, N. M., and Power, M. H.: The Urinary Excretion of Sucrose and Its Distribution in the Blood After Intravenous Injection Into Normal Men, *Am. J. Physiol.* 120: 203, 1937.
19. Leviets, P. H., Bondillon, J., and Klinghoffer, K. A.: The Volume of the Extracellular Fluids of the Body, *J. Clin. Investigation* 15: 261, 1936.
20. Unpublished results.
21. Graef, I.: Discussion, *Arch. Path.* 27: 947, 1939.
22. Hamilton, W. F., Brewer, G., and Brotman, I.: Pressure Pulse Contours in the Intact Animal, *Am. J. Physiol.* 107: 427, 1934.
23. Katz, L. N., Friedman, M., Rodbard, S., and Weinstein, W.: Observations on the Genesis of Renal Hypertension, *Am. Heart J.* 17: 334, 1939.
24. Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension, *J. Exper. Med.* 59: 347, 1934.
25. Unpublished results.
26. Keith, N. M., Power, M. H., and Patterson, R. D.: The Distribution and Recovery of Intravenously Injected Sucrose, *Am. J. Physiol.* 109: 62, 1934.
27. Phillipsborn, H. F., Katz, L. N., and Rodbard, S.: The Effect of High Protein Diets on Experimental Renal Hypertension, *J. Exper. Med.* 74: 591, 1941.
28. Ellis, L. B., and Faulkner, J. M.: Circulatory Effects of Intravenous Injection of 50 Per Cent Dextrose and Sucrose Solutions in Patients With Heart Disease, *Am. Heart J.* 17: 542, 1939.
29. Rigdon, R. H., and Cardwell, E. S.: Renal Lesions Following Intravenous Injection of a Hypertonic Solution of Sucrose, *Arch. Int. Med.* 69: 670, 1942.

doubtful. Cirroid and arteriovenous aneurysms are quite different from the condition we are studying. At least some of the cases of post-traumatic aneurysm differed from pulsating hematomas only in duration. It is well known that syphilis causes aneurysms of only the great vessels; no case of temporal aneurysm has been considered of syphilitic origin. There have been other recent reports but we have been unable to find records of any cases of spontaneous true aneurysm of this artery other than the nine listed by Winslow and Edwards.

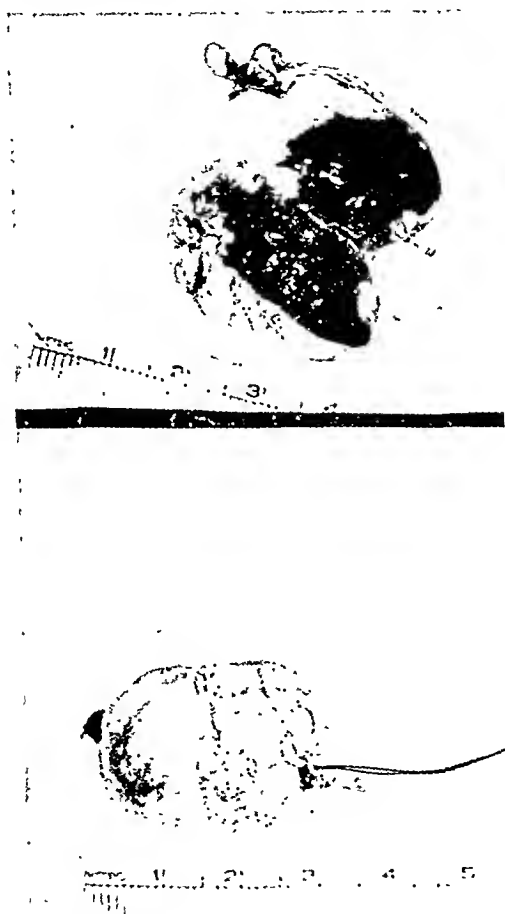


Fig. 3.—Photographs of the pathologic specimen whole (below) and bisected (above), and a centimeter rule.

CASE REPORT.—E. W., male, Caucasian, aged 34 years, was admitted to the hospital, May 6, 1929. About five years before, the patient had noticed a small swelling just in front of the right ear. The size increased with gradual acceleration; it was only about one-half its present size a year before. There was no pain and no symptom of any kind other than the presence of tumor. The size seemed to decrease somewhat with rest. There were no history of injury, no illnesses during the past ten years, no venereal infections. In 1929, he was in another



Fig. 1.—Photographs of E. W. before operation.

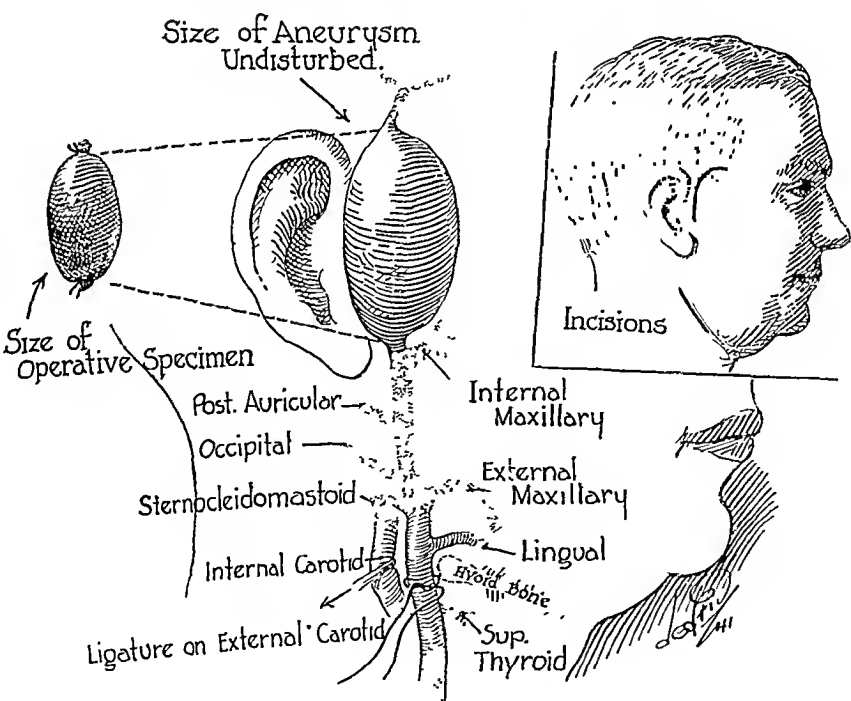


Fig. 2.—Schematic drawing showing in solid lines the vessels that were seen at operation.

The dressings were padded with cotton and a firm figure-of-eight bandage was applied about the head and neck.

The convalescence was uneventful. Four days after operation the larger skin stitches were removed and the patient was allowed to leave the hospital. There were no symptoms or signs of local circulatory deficiency nor was there any interference with nerve function.

The pathologic specimen measured 3.2 by 2.1 by 2.1 cm. (Fig. 3). It contained recent blood clot. Microscopic sections of the wall of the aneurysm showed uniformly thinned media (Fig. 4).

DISCUSSION

The patient presented himself for treatment only because of the enlarging tumor; there was no pain and no other symptom. Operative incisions were placed to give adequate exposure and at the same time leave no noticeable scars. It might seem that the neck operation with ligation of the external carotid was unnecessary. The rapid filling of the aneurysm after compression and the proximity of the facial nerve led us to take this precaution. Ligation distal to the origin of the lingual artery probably would have reduced the blood flow into the sac more effectively.

The extreme elasticity of the thin-walled aneurysm was a striking feature of the operative findings. The volume of the specimen as it was removed was apparently only about one-third the volume of aneurysm before interference (Fig. 2). The sac was immediately surrounded by loose connective tissue; its removal was easy.

SUMMARY

Aneurysm of the temporal artery is a rare condition which is usually post-traumatic. Our case of spontaneous true aneurysm is apparently the tenth case of its kind to be reported. Cure was easily and safely effected by excision after ligation of the external carotid artery.

REFERENCES

- De Santi, L.: Des tumeurs anév. de la région temporelle, *Arch. gén. de méd.*, Par. 2: 7.s., 14: w.s., 154: 543 and 679, 1884; also *Arch. gén. de méd.*, Par. 1: 7.s., 15: w.s., 155: 172, 1885.
Winslow, Nathan, and Edwards, Monte: Aneurysm of the Temporal Artery, *Bull. School Med. Univ. Maryland* 19: 119, 171, 1935.

hospital for drainage of a small submental "abscess" and for circumcision. The only other known illness was scarlet fever at the age of 4 years.

Physical examination showed nothing remarkable except for the tumor which measured about 5.7 by 3.0 by 2.5 cm. (Fig. 1). There were no visible pulsations but upon palpation a definite expansile pulse was felt. It was not attached to the skin. The upper pole could be moved a little over the temporal fascia and the zygoma, but the lower pole seemed fixed. There was no audible bruit. Upon pressure, it would disappear; when released, it would expand again quickly (perhaps one to two seconds) with a soft palpable swish.

The blood pressure readings were 136/78 and 110/82. The laboratory studies, including complement fixation tests for syphilis, were negative.

Operation was performed with open cone ether anesthesia. Using the great horn of the hyoid bone as a guide, an oblique incision was made in one of the skin creases of the neck. Both the internal and external carotid arteries were exposed. After demonstrating that compression of the external carotid made the aneurysm softer and slower in refilling, it was ligated with black silk No. 8 (Fig. 2).



Fig. 4.—Photomicrograph of the wall of the aneurysm.

A second incision was curved over the superior and posterior surfaces of the aneurysm with its lower end just in front of the tragus. The aneurysm was situated superficial to the zygomatic process of the temporal bone, extending up over the temporal fascia, and down into the parotid gland. It was of the fusiform type, thin-walled throughout and very elastic. The artery above was clamped, ligated, and severed. Then, while deep pressure was applied with a finger behind the neck of the mandible in the region of the bifurcation of the external carotid artery, the aneurysm was easily isolated by sharp and blunt dissection. The only arterial communications were at the upper and lower poles; no auricular, transverse facial, or zygomatico-orbital branches were seen (Fig. 3). The artery at the lower pole of the aneurysm was also ligated with black silk No. 8.

The wound of the face was closed by stitching the subcutaneous layer with fine plain catgut and the skin with black silk. The wound in the neck was closed by sewing the platysma with chromic No. 00 and the skin with black silk.

ileum and the ascending colon. Similar operations were attempted by Billroth in 1881, and von Bergmann in 1882, but it remained for Maydl, in 1883, to perform the first successful resection of the cecum. In his case, resection was preceded by ileostomy, which, six months later, was converted into an ileocolonic stoma. The patient died in the course of a year from recurrence. The next year Billroth reported a successful case in which primary end-to-end anastomosis had been performed; in 1885, similar reports were published by Hofmohl and by von Bergmann. Barton, in 1888, was the first to report successful resection in this country, but he was never able to rid his patient of the artificial anus which he had established.

As more of these operations were performed, it soon became apparent that they left much to be desired. This was true of operations on all portions of the colon. In 1889, Franks collected fifty-two cases of "colectomy" from the literature and found that the mortality rate was 40.8 per cent. His studies led him to conclude that, because of the poor survival rate, the operation was a failure as a curative agent for malignant disease but that it should be performed whenever possible because of the symptomatic relief it afforded. As he found no difference between the mortality rate following immediate suture and that following establishment of an artificial anus, he advocated closure in order to eliminate a second operation.

Recognition of these poor results led to an active search for better methods of handling the problem. The chief hazards were peritonitis and shock. Some of the early operations took four or five hours to perform and required innumerable sutures, which defeated the purpose that they were intended to serve. Contamination might occur at the time of operation as a result of accident or careless technique, or, later, because of a faulty suture line. Efforts toward improvement by a quick, safe method lay in several directions. The first was to keep all manipulations of the bowel outside the peritoneal cavity. This was the principle of exteriorization, employed of necessity by Maydl, Schull, and von Volkmann, of design by Bloch, Paul, and von Hochenegg and publicized by Mikulicz. It found its widest application in operation for lesions situated in the sigmoid, but it recently has been warmly advocated by Lahey and his associates in operation for lesions in the right half of the colon as well. The relative speed and simplicity of this type of operation also aided in reducing the occurrence of shock. However, those who found the idea of an artificial anus repellent strove to find a method which would combine the safety and speed of exteriorization with the obvious advantages of primary anastomosis. The old method of suture was felt to be too time-consuming and uncertain. Countless tricks and gadgets were tried to facilitate anastomosis. Among these were McGraw's elastic ligature, Murphy's button, Madelung's cartilage plates, Seim's bone plates, Ullman's carrot bobbin, Pileher's potato bobbin, Starr's rubber

END-TO-END ILEOCOLOSTOMY: INDICATIONS FOR, AND EVALUATION OF, IN RESECTION OF RIGHT PORTION OF COLON IN ONE STAGE FOR MALIGNANT LESIONS

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IT IS generally agreed that the procedure of choice in dealing with operable malignant lesions of the right portion of the colon is radical removal of that portion of bowel which lies between the terminal portion of the ileum and the middle of the transverse colon, together with removal of the associated gland-bearing tissues. However, agreement as to the best means of accomplishing this end safely and expeditiously and of restoring continuity of the bowel is not general. It is our belief, as it is the belief of many other surgeons, that it is futile to attempt to standardize resection of the right portion of the colon and the procedure to be carried out must be adapted to the patient. We consider as unsound all dogmatic statements made in regard to the questions of whether operation should be carried out in one, two, or more stages, the type of anastomosis that should be established, and the type of suture that should be employed. Advocates of various methods are in the habit of ascribing such success as they have achieved to some particular measure which they have devised or employed. Actually, success in management of these cases depends on a multitude of factors, including selection of patients and preoperative and postoperative care. Surgeons are ill advised who feel that one particular step or method is all important or indispensable.

It is our purpose to review briefly the background of the problem and to describe a method of operation which we have found satisfactory in certain cases.

BACKGROUND

Early resection of the colon was less radical than that customarily employed today and consisted of resection of the tumor-bearing region and immediate performance of end-to-end anastomosis. In 1879, Baum carried out such a procedure for a lesion of the ascending colon in a case in which ileostomy had been performed for obstruction eight weeks previously. The patient died nine days after resection was performed. Later in the same year, Kraussold removed the ileocecal coil from a patient for carcinoma and performed anastomosis between the terminal portion of the

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taking study of the lymph vessels and nodes in this region. They advocated removal of all glands receiving direct vessels up to the gland by the duodenum at the origin of the ileocolic artery, which they felt was the highest "primary" gland.

VARIOUS PROCEDURES

Although the actual resection of the colon now has become well standardized, the remainder of the operation has not, since it may be performed in one, two, or more stages and by various types of technique. A brief review of these methods with some of their advantages and disadvantages may be worth while.

Operation in Multiple Stages.—Operation in multiple stages, including exteriorization of the segment of bowel which contains the growth, removal of this segment, application of clamps to the spur, and closure of the residual stoma, has been practiced most widely at the Lahey Clinic. Carter, Slattery, and Hahn, Patterson and Webb, and others have written of its virtues. It was stated that it afforded the least danger of peritonitis and the greatest safety to the patient, since there is no fear of leakage or contamination. According to Lahey, the large bowel, because of its sacculated walls, scanty blood supply, virulent bacteria, bands and appendages, is unfavorable for suture. Exteriorization probably is the simplest method of handling the problem, but the results have not been too successful in all hands. The excoriating ileal discharges, the degree of infection of the wound, the incidence of postoperative hernia, the long morbidity, and the necessity for many operations have led many to condemn it. Rankin²⁸ stated that the Mikulicz procedure is followed by recurrence in the abdominal wall in 12 per cent of cases. The limitations of the method were described by Sistrunk, who pointed out that it was applicable only to mobile or easily mobilized parts associated with a resectable mesentery, and that it was not suitable for large or adherent growths with infection or those associated with obstruction. Similarly, it was technically unsatisfactory in cases in which the patients were obese or in which a short mesentery was present. When used in such cases, carcinoma or infection was likely to invade either the wound or the peritoneal cavity.

Operation in Two Stages.—Wakeley and Rutherford stated that lateral ileocolostomy followed by resection ten to fourteen days later is the correct procedure for growths situated in the right portion of the colon. Many surgeons agree. Pemberton and Whittaker felt that such a course lowered the mortality rate and increased the operability. Infection about the growth subsides and obstruction is relieved after diversion of the fecal current. There is less reaction after resection as this is carried out in a separate compartment, formed by the adhesions of the first operation. Dixon and Priestley stated that the severity and shock of the operation are reduced by the two-stage procedure and that the second operation

tube, invagination rings and so forth. The extent to which these devices aided in making anastomosis safer is attested by such studies as that of Magill, who, in 1894, made the first thorough review of the literature on resection of the ileocecal coil. He found that the mortality rate was lowest in the hands of surgeons who used these devices and that the mortality rate and incidence of fecal fistula were highest in cases in which suture anastomosis was employed. Littlewood found that anastomosis could be performed in ten to fifteen minutes, in contrast to the lengthy earlier operations.

As these devices simplified anastomosis and, by their function, minimized late leakage, attempts were made to reduce the last major hazard, namely, contamination of the peritoneal cavity with contents of the bowel at the time of operation. This was the search for a completely aseptic anastomosis. Initiated by the experiments of Halsted, in 1887, the crusade was carried on with the suture overlamp method of O'Hara, the Parker Kerr basting stitch, and the countless modifications of aseptic clamps which Rankin and others²⁹ have devised.

The final road along which safety in operations on the right half of the colon was sought was the operation in multiple stages. Following the first successful exclusion by Trendelenburg in 1885, this operation was employed at first only as a palliative measure to circumvent obstruction. Later it was performed as a preliminary step to subsequent resection. By this method the unpleasant features of an artificial anus were avoided, and, by establishing anastomosis at one operation, resection subsequently became less hazardous.

As more patients began to survive the operation and to die from recurrence, the cause for the failure of resection to effect a cure was sought. In the early operations, only the growth and the immediately adjoining portions of bowel were removed. By taking out more bowel and exercising care to remove adjacent lymph nodes, it was found that the survival rate could be increased. The present pattern for resection was established by Friedrich, in 1904. He advocated removal of several inches of the terminal portion of the ileum, the cecum, appendix, the ascending colon, hepatic flexure, and the first third of the transverse colon, along with the regional lymph nodes. Friedrich performed this operation in one stage, uniting the terminal portion of the ileum to the transverse colon by a side-to-side isoperistaltic anastomosis. The rationale of this type of procedure was summarized by Cheever, in 1931. He pointed out that removal of a smaller portion of the colon did not give a wide enough margin of safety, that the proximal portion of colon, being incompletely covered by peritoneum, was less amenable to anastomosis, that the rich blood supply of the ileum minimized the liability to necrosis at the suture line, and that the operation was relatively easy. The importance of radical removal of the ileocolic lymph vessels and nodes en masse with the growth was emphasized by Dobson and Jamieson, who made a pains-

measure in cases in which the patient is debilitated and bleeding and who probably could not stand more than one operation. Rankin,²⁸ Jones,¹⁴ Wangensteen, Campbell, MacFee, and Stone and McLanahan have advocated anastomosis by the so-called aseptic technique. Bell and Henley and many other surgeons now perform open anastomosis, occasionally employing a basting stich.

Continuity of the bowel may be restored by end-to-end, end-to-side, or side-to-side anastomosis. Each method has its advocates; Allen stated that this consideration is of no importance. End-to-end anastomosis is technically the simplest to perform; there is only one suture line and no blind ends are left. It has been stated that leakage is likely to occur at the mesenteric juncture because the space where the mesentery splits is devoid of peritoneum, but, according to Rankin and co-workers,²⁹ faulty cutting or clamping, without adequate regard of blood supply, more often is the real cause of leakage.

It has been stated that side-to-side anastomosis forms the strongest anastomosis and that vascularity is assured by supplement from the ileum. On the other hand, the blind ends, especially if left too long, may form reservoirs for the accumulation of waste. Whether the abolition of peristalsis produced by cutting the circular muscle fibers is of practical importance is doubtful.

The end-to-side anastomosis is said to simulate most nearly the normal ileocolic relationship. In operations carried out in more than one stage, it affords better bypassing of the fecal current but may prove dangerous if obstruction develops.

Each of these methods has its proper place. It is when one method only is employed, to the exclusion of others, that an injustice is done to the patient.

In the presence of acute perforation or in certain cases in which a lengthy operation would tax unduly the strength of a seriously ill patient, exteriorization and the operation performed in multiple stages can be used to great advantage. In cases of localized perforation and high grades of infection, preliminary short circuiting greatly facilitates and adds to the safety of subsequent resection. When obstruction exists, preliminary decompression is the primary consideration. If this cannot be achieved by medical means and if dilatation is not great, the bowel should be decompressed by a short circuiting operation. If distention is great, ileostomy or cecostomy are the procedures of choice. Under no circumstances should resection in one stage be carried out under such conditions, and, in the presence of a dilated, edematous bowel, undue manipulation and attempts at anastomosis are unwarranted. However, in the case of a patient who is well prepared preoperatively, who seems to be standing the procedure well, and whose growth is found to lend itself readily to resection, we feel that resection and anastomosis in one stage is the ideal course to follow. As to the means by which anastomosis

is safer because of autovaccination which takes place during the first procedure. They pointed out that if death occurs after resection in one stage, it is questioned, in retrospect, whether a procedure of less magnitude could have been adopted. Although this is true, questions also arise when death occurs after operation in two stages. Ransom, in reviewing the material at the University of Michigan, concluded that operation in two stages was the safest procedure, since the amount of manipulation carried out at one time was less. He found that the time involved actually was not any longer because these patients had a smoother convalescence, and, since malignant tumors of the colon were slow growing, there was no added hazard because the tumor was left in the body longer. Allen reached a similar conclusion on reviewing the material at Harvard University. Rankin²⁸ felt that in any event it was the best procedure for surgeons who did not have special training in this field. On the other hand, Lovelace and one of us (C. W. M.),²¹ in a review of 885 cases encountered at the Mayo Clinic, in 67 per cent of which resection was carried out, found that the mortality rate was 6.7 per cent higher and the hospital stay twenty-four days longer following operation in two stages than in cases in which operation was carried out in one stage. The low mortality rate reported by the numerous advocates of operation in two stages may be owing to their failure to include deaths which occurred after the first stage of the operation. Furthermore, the short interval between stages advised by numerous writers is seldom feasible in actual practice.

Operation in One Stage.—Operation in one stage is the operation of pioneers in this field. Condemned for many years because of its dangers, the trend now is back toward it, as Rankin²⁸ pointed out, because of the better preparation and selection of cases and the increasing experience of surgeons. Moynihan, Wilkie, and Lockhart-Mummery in Great Britain, and Harvey, Andrews, Cheever, and MacFee in this country, have advocated its use widely. Rankin²⁸ stated early that it was applicable in about one-half of the cases without increased risk. Stone and McLanahan, who formerly advocated operation in more than one stage, now favor operation in one stage.

The advantages of operation in one stage are many. The patient is subjected to only one operation and one anesthesia, with their attendant risks. Stay in the hospital is shorter and the time that the tumor remains in the body is reduced. This, according to Lovelace and one of us (C. W. M.), is reflected in an increase of 2.5 per cent in the five-year survival rate. Resection is technically easier since the surgeon is unhampered by the adhesions of a previous operation. Since resection has to be performed, it might as well be at the first operation, as restoration of continuity of the intestinal tract constitutes only a minor part of the operation. Although most of its advocates urge its use for patients in good condition, there are those who would use it only as a palliative

measure in cases in which the patient is debilitated and bleeding and who probably could not stand more than one operation. Rankin,²⁸ Jones,¹⁴ Wangersteen, Campbell, MacFee, and Stone and McLanahan have advocated anastomosis by the so-called aseptic technique. Bell and Henley and many other surgeons now perform open anastomosis, occasionally employing a basting stitch.

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should be carried out, the findings of Lovelace and one of us (C. W. M.) are of interest. In a review of the cases in which resection in one stage was performed at the Mayo Clinic, it was found that the mortality was 23.4 per cent when end-to-side anastomosis was performed; 22.7 per cent when side-to-side anastomosis was performed, and 19.2 per cent when end-to-end anastomosis was carried out. It is this finding that prompted our interest in this technique and led to the present study.

It long has been felt that if operation in one stage is performed, a safety valve should be provided by performing enterostomy to insure against tension on the suture line caused by the collection of gas and waste. This has been an almost inviolable rule with Rankin and associates,²⁹ Jones,¹⁵ and Judd. Stone and McLanahan found it seldom performed in their series of cases but felt that it should be performed more often. Cheever felt that it did no harm. Wilkie and Lockhart-Mummery felt that it might be better to perform an operation in two stages rather than perform enterostomy. Harvey condemned the procedure as a source of infection and fecal fistula from leakage around the tube; he felt that an inlying rectal tube came nearer to accomplishing the desired result. Ransom found a much higher mortality rate in both palliative and curative operations when enterostomy was performed. Lovelace and one of us (C. W. M.) reported a similar observation.

CASES IN WHICH END-TO-END ILEOCOLOSTOMY WAS PERFORMED AT THE • MAYO CLINIC

The present study is based on a review of all cases encountered at the Mayo Clinic in which resection of the right portion of the colon with end-to-end anastomosis of the ileum and colon was carried out for malignant disease. Ninety-six such operations were performed by eight surgeons prior to Jan. 1, 1942. There were eighteen hospital deaths, a gross mortality rate of 18.8 per cent. The average stay in the hospital of patients surviving operation was 20.3 days. In forty-two cases, Witzel enterostomy was carried out as a "safety" measure. The mortality rate in this group was 28.6 per cent. The average stay in the hospital was 22.5 days. In the fifty-four cases in which enterostomy was not established, the mortality rate was 11.1 per cent and the average stay in the hospital was 18.9 days (17.7 days if one patient who stayed in the hospital seventy-seven days is excluded).

This operation was used most frequently at the clinic in the decade of 1917 to 1927. However, as the surgeons became wrongly but increasingly aware of the need for enterostomy, the mortality rate increased until the operation finally was discarded; only two such operations were performed in the next ten years. However, as a result of the review by Lovelace and one of us (C. W. M.), it again has come into frequent use, but without supplementary enterostomy. At the time of this writing, this operation

has been carried out in twenty-seven cases on the service of one of us (C. W. M.) with only one death, that of a man 82 years of age.

Technique of Operation.—The anesthesia is adapted to the patient; in most cases spinal anesthesia, supplemented by pentothal sodium, is found satisfactory. The abdomen is opened by a right rectus incision, the muscle being retracted mesially within its sheath. The liver is palpated carefully for evidence of metastasis. Metastasis is found in about 10 per cent of cases of carcinoma of the right portion of the colon in which exploration is performed. The entire colon then is examined in order to determine whether other tumors are present. They may be expected in about 6 per cent of the cases. The lesion then is examined carefully and its size, situation, and mobility are determined. Regional lymph nodes should be palpated, although the decision as to their involvement rests with the pathologist. Resection then should be planned so that in its execution there will be no difficulty in effecting adequate removal and subsequent anastomosis.

The cecum is elevated and retracted mesially, and mobilization of the right portion of the colon is effected by incision of the lateral peritoneal reflection. By blunt dissection the colon and its mesentery are mobilized almost to the midline, care being exercised to avoid injury to the retroperitoneal portion of the duodenum and the right ureter. A wide segment of mesentery is resected to remove the lymph vessels and nodes draining this region. The mobilized segment of bowel is placed outside the peritoneal cavity and is walled off with moist sponges. The ileum and transverse colon are cut across; usually about 6 inches (15 cm.) of ileum and about a third of the transverse colon are removed. For lesions of the hepatic flexure, more of the transverse colon is removed. The segments to be used for anastomosis are grasped with rubber-shod clamps and division is effected with the cold knife. The use of crushing clamps or cautery on segments to be used for anastomosis seems inadvisable as anastomosis is more likely to succeed in healthy normal tissue than when crushed tissue with thrombosed blood vessels is used. As emphasized by Loekhart-Mummery, both the large and small bowel should be divided obliquely. The small bowel is divided obliquely in order to compensate for the disparity in size which exists between it and the large bowel; the large bowel is divided this way in order to insure an adequate blood supply to its entire circumference. If the opening in the ileum requires further enlargement, this can be achieved by a longitudinal cut along the antimesenteric border, the edges being rounded off. The mucosa is swabbed with tincture of mercuric iodine.

The rubber-shod clamps are approximated, the wound is walled off carefully with moist sponges, and the posterior row of sutures is inserted in the form of a continuous silk stitch. The posterior suture of catgut in the mucosa then is inserted, the corner is rounded carefully, and the anterior borders are approximated with an inverting stitch of the base-

ball variety. The rubber-shod clamps are removed and the outer row of silk sutures are inserted. Nearby epiploic tags are drawn over the anastomosis for added security. The cut edges of the mesentery are approximated, care being taken not to jeopardize the blood supply at the line of the anastomosis. The raw surface of the interior portion of the abdominal wall is then covered with peritoneum as well as possible. Raw surfaces and traps should be eliminated. *In ideal cases drainage is unnecessary.* In the usual case, one or two soft rubber drains are inserted through a stab wound in the right flank into the retroperitoneal space. Occasionally a strand of silk is left attached at the site of anastomosis and is brought out through the abdominal incision to serve as a guide for drainage. Tincture of mercuric iodine is used liberally, and, recently, it has been our practice to insert 75 gr. (5 Gm.) of sulfanilamide powder into the peritoneal cavity before closure. Before the patient is taken from the operating room, the anal sphincter is temporarily paralyzed by thorough dilatation. This procedure has been found to be as effective as an inlying rectal tube in preventing retention of gas and feces by the sphincter.

The following variations were noted. Anastomosis by the aseptic method was performed in three of the ninety-six cases. Many of the aseptic methods are complex and time consuming. The designation "aseptic" may lull the surgeon into a false sense of security and cause him to forget more important fundamentals. Even after aseptic anastomosis, bacteria usually can be cultured from the line of suture. Crushing and burning tissue does not enhance its value for anastomosis. The sutures are carefully placed, including, as Halsted demonstrated, the submucosa in each stitch and avoiding large numbers of sutures. As Wilkie pointed out, numerous sutures kill tissue and furnish a culture medium for anaerobes. Avoidance of tension, judicious reinforcement, and, especially, attention to blood supply accomplish more than employment of a multitude of gadgets. Late leaks, rather than contamination at the time of operation, account for most deaths. In one of the early cases, anastomosis was carried out over a rubber tube.

Perforating growths often require more extensive resection. Part of the abdominal wall had to be removed in three cases and the parietal peritoneum in a large number. Several feet of adherent ileum were removed in three cases and a loop of sigmoid was removed in another. In two cases resection of outer coats of the duodenum and portions of the pancreas was performed. Additional procedures, such as herniorrhaphy, myomectomy, and insertion of a tube for radium were carried out in one case each. In seventy-six cases, however, the operation was carried out largely as described, and it was only in the early cases that the most complicated situations were treated in one stage.

As pointed out previously, enterostomy was carried out almost routinely in many of the early cases. We feel, however, that enterostomy

not only is unnecessary but actually is hazardous and adds greatly to the risk of operation. If the surgeon does not like the appearance of the bowel or does not trust the anastomosis, he should perform the operation in multiple stages and not feel that everything is set aright by placing a tube in the ileum.

When we discovered the striking differences in mortality rates which existed in the cases in which enterostomy had been performed and those in which it had not, we thought perhaps this might be due to the fact that enterostomy had been performed on the patients who were sicker, who had obstruction, or who had undergone extensive operations. A review of the cases disclosed that this was not true, that the two groups were comparable in every way, and that the only factor which should be held accountable for the increase of 17.5 per cent in the mortality rate was the enterostomy. As a substitute for enterostomy, it is advisable to dilate the anus thoroughly immediately after operation in order to paralyze temporarily the external sphincter.

Selection of Cases and Findings at Operation.—In the early days of the operation there seems to have been little selection of cases. The operation to be performed depended largely on the whims or inclination of the surgeon; whether he added enterostomy was largely a matter of personal conviction, some surgeons performing it routinely and others occasionally.

The patients in this series of cases were between 15 and 81 years of age; the average age was 53.9 years. Sixty-seven of the patients were men and twenty-nine, women. At the time of operation, fifty-eight patients were thought to be in good general condition, fourteen in fair condition, and twenty-four in poor condition. Complicating conditions, such as goiter, old tuberculosis, cardiac disease, or arteriosclerosis, were present in fifty-one cases. Two patients had amebic dysentery and eleven had undergone abdominal operations within six months previous to operation. A toxic goiter was removed from one patient a week before operation on the colon was performed. Obesity was marked in several cases; nearly all patients had anemia of some degree and a third had severe anemia. Half of those who had severe anemia required transfusion before operation. Many patients had lost weight, a fourth of them having lost more than twenty-five pounds (11.3 kg.). Slight evidence of obstruction was noted in four cases and eight patients gave a history of recurrent obstruction.

The tumor was a carcinoma in ninety-three cases and a sarcoma in three. The lesion was situated in the cecum in fifty-nine cases, in the ascending colon in twenty-eight, and in the hepatic flexure in nine. In 51 per cent of cases there was neoplastic extension through the wall of the bowel which had involved the serosa, abdominal wall, or adjacent bowel. Inflammatory fixation had occurred in sixteen more cases, so that in only thirty-one cases was the growth freely movable and of type A, according

ball variety. The rubber-shod clamps are removed and the outer row of silk sutures are inserted. Nearby epiploic tags are drawn over the anastomosis for added security. The cut edges of the mesentery are approximated, care being taken not to jeopardize the blood supply at the line of the anastomosis. The raw surface of the interior portion of the abdominal wall is then covered with peritoneum as well as possible. Raw surfaces and traps should be eliminated. In ideal cases drainage is unnecessary. In the usual case, one or two soft rubber drains are inserted through a stab wound in the right flank into the retroperitoneal space. Occasionally a strand of silk is left attached at the site of anastomosis and is brought out through the abdominal incision to serve as a guide for drainage. Tincture of merthiolate is used liberally, and, recently, it has been our practice to insert 75 gr. (5 Gm.) of sulfanilamide powder into the peritoneal cavity before closure. Before the patient is taken from the operating room, the anal sphincter is temporarily paralyzed by thorough dilatation. This procedure has been found to be as effective as an inlying rectal tube in preventing retention of gas and feces by the sphincter.

The following variations were noted. Anastomosis by the aseptic method was performed in three of the ninety-six cases. Many of the aseptic methods are complex and time consuming. The designation "aseptic" may lull the surgeon into a false sense of security and cause him to forget more important fundamentals. Even after aseptic anastomosis, bacteria usually can be cultured from the line of suture. Crushing and burning tissue does not enhance its value for anastomosis. The sutures are carefully placed, including, as Halsted demonstrated, the submucosa in each stitch and avoiding large numbers of sutures. As Wilkie pointed out, numerous sutures kill tissue and furnish a culture medium for anaerobes. Avoidance of tension, judicious reinforcement, and, especially, attention to blood supply accomplish more than employment of a multitude of gadgets. Late leaks, rather than contamination at the time of operation, account for most deaths. In one of the early cases, anastomosis was carried out over a rubber tube.

Perforating growths often require more extensive resection. Part of the abdominal wall had to be removed in three cases and the parietal peritoneum in a large number. Several feet of adherent ileum were removed in three cases and a loop of sigmoid was removed in another. In two cases resection of outer coats of the duodenum and portions of the pancreas was performed. Additional procedures, such as herniorrhaphy, myomectomy, and insertion of a tube for radium were carried out in one case each. In seventy-six cases, however, the operation was carried out largely as described, and it was only in the early cases that the most complicated situations were treated in one stage.

As pointed out previously, enterostomy was carried out almost routinely in many of the early cases. We feel, however, that enterostomy

monary infarction in the other. In one of these two cases, enterostomy had been performed. One man, 82 years of age, died of bronchopneumonia.

SUMMARY AND CONCLUSIONS

There are many methods for dealing with carcinoma of the right portion of the colon. We have reviewed a number of these methods, together with their background and development. Resection with end-to-end ileocolostomy in one stage is a method which has been found satisfactory in certain cases. This operation has been performed at the Mayo Clinic ninety-six times, with eighteen deaths. In forty-two cases complementary enterostomy was performed; the mortality rate in this group was 28.6 per cent. In the fifty-four cases in which enterostomy was not performed the mortality rate was 11.1 per cent. We now regard enterostomy not only as unnecessary but also as an added hazard in conjunction with resection and anastomosis in one stage. If the surgeon has any misgivings, operation in two stages is preferable to the performance of enterostomy.

REFERENCES

1. Allen, A. W.: Right Colectomy for Malignant Disease; a Discussion of the Mortality Associated With Various Operative Procedures, *J. A. M. A.* 109: 923-928, 1937.
2. Andrews, Edmund: Carcinoma of the Cecum; Partial Colectomy and End-to-End Anastomosis, *S. Clin. North America* 11: 111-116, 1931.
3. Barton, L. M.: Epithelioma of the Ileo-cecal Valve; Resection of Three Inches of Intestine; Recovery, *J. A. M. A.* 10: 549-550, 1888.
4. Bell, H. G., and Henley, R. B.: Right Colectomy in One Stage, *Surgey* 8: 94-97, 1940.
5. Campbell, O. J.: Surgery of Carcinoma of the Colon, *Minnesota Med.* 23: 215-219, 1940.
6. Carter, R. F., Slattery, L. R., and Hahn, R. C.: Adaptation of the Mikulicz Operation for the Right Colon and Rectosigmoid, *Ann. Surg.* 111: 80-92, 1940.
7. Cheever, David: The Choice of Operation in Carcinoma of the Colon, *Ann. Surg.* 94: 705-716, 1931.
8. Dixon, C. F., and Priestley, J. T.: Factors Which Decrease Risk in Operations on the Colon and Rectum, *Surg., Gynec. & Obst.* 57: 206-212, 1933.
9. Dobson, J. F., and Jamieson, J. K.: Excision of the Cecum and Ascending Colon With the Corresponding Lymphatic Area, *Lancet* 1: 149-151, 1908.
10. Franks, Kendal: Colectomy or Resection of the Large Intestine for Malignant Disease, *Tr. Roy. Med.-Chir. Soc. Glasgow* 72: 211-232, 1889.
11. Friedrich, P. L.: Prinzipielles zur operativen Behandlung der Flacciditumoren, gleichzeitig ein Beitrag zur Symptomatik der Invagination Cœci in Colon transversum, *Arch. internat. de chir.* 2: 231-245, 1904.
12. Halsted, W. S.: *Surgical Papers by William Stewart Halsted*, Baltimore, 1928, Johns Hopkins Press, vol. 1, 586 pp.
13. Harvey, S. C.: The One-stage Operation for Resection of the Cecum and Proximal Colon, *New England J. Med.* 211: 1039-1044, 1934.
14. Jones, T. E.: The Treatment of Cancer of the Colon, *Surg., Gynec. & Obst.* 62: 415-419, 1936.
15. Jones, T. E.: Treatment of Carcinoma of the Colon, *S. Clin. North America* 19: 1123-1134, 1939.
16. Lahey, F. H.: Neoplasms of the Cecum and Ascending Colon, *Am. J. Surg.* 46: 3-11, 1939.
17. Littlewood, H.: A Successful Case of Ileo-sigmoidostomy (Senn's method) for Intestinal Obstruction Due to Malignant Disease of the Hepatic Flexure of the Colon; With Some Remarks on Intestinal Anastomosis and a Description of a modification of Senn's Bone Plates, *Lancet* 1: 864-866, 1892.

to Dukes' classification. Regional nodes were involved by metastatic implants in 52 per cent of the cases. There was questionable involvement of the liver in three cases and definite involvement in one. In eighty-nine cases operation was performed with the hope of cure; in seven cases operation was palliative because of involvement of lymph nodes, local peritoneal extension which could not be removed, or metastatic deposits in the liver. Adenomatous polyps were noted in three cases, in one of which malignant degeneration had occurred. Metastatic nodules were found in the mucosa of the ileum, cecum, and ascending colon in one case. At the time of operation the small intestine was dilated in eight cases and the large intestine in one.

In general, care in the selection of cases has increased. Patients should be in fairly good general condition and should not have objective evidence of obstruction or of marked inflammatory reaction about the growth if operation is to be performed in one stage.

Preoperative and Postoperative Care.—In the early cases, the patients were admitted to the hospital, given an enema, and, occasionally, a dose of castor oil and then submitted to operation. Now great care is taken to cleanse the bowel and to improve the general condition of the patient. When resection in one stage is anticipated, vaccine is given intraperitoneally. After operation each patient is placed in an oxygen tent and given 500 c.c. of citrated blood. Fluids are administered parenterally, the oral route being prohibited until the patient begins to pass gas by rectum. Frequent insertion of glycerin suppositories and tubes into the rectum facilitates the passage of gas.

Complications.—Infection of wounds was the most common complication among the patients who survived operation; it occurred in twenty-eight cases. Infection of wounds has been less frequent since the use of sulfanilamide. This and other complications were common among patients who underwent enterostomy. Fecal fistula developed in only two cases. All fistulas caused by enterostomy tubes closed spontaneously. Pulmonary complications were infrequent among patients who survived operation; atelectasis and pneumonia occurred in one case each, and pulmonary infarction in two cases. Ileus occurred in three cases, in one of which it was necessary to perform ileostomy. Cystitis was noted in seven cases. Low grade inflammatory processes about the site of an anastomosis, which gradually disappeared, occurred in three cases. Parotitis developed in three cases and submaxillary mumps in one.

Cause of Death.—General peritonitis was the most common cause of death in the series. It accounted for fifteen of the eighteen fatalities. In two of these cases, pneumonia also was present and in one, pulmonary embolism occurred. In eleven of these fifteen cases, ileostomy had been performed. Local peritonitis was the cause of death in two cases; it was associated with ileus in one case and with acute endocarditis and pul-

DOUBLE LOOP RECTAL RESECTOR AND BIOPSY FORCEPS

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THE instrument illustrated in Fig. 1 is designed for the endoscopic electric resection of rectal papilliferous new growths as well as for the removal of specimens for histologic studies. This instrument is especially useful for the extirpation of large, broad, sessile adenomas when the looping of the pedicle with the ordinary single wire loop snare is either technically impossible or unsafe.

The instrument consists of a pair of removable tungsten wire loops mounted at the distal end of an insulated shaft and actuated by forceps handles. The proximal loop transmits the cutting current and meshes into the stationary, inactive distal loop which is slightly larger. The proximal loop travels a maximum longitudinal distance of 2 cm. parallel to the shaft of the instrument.

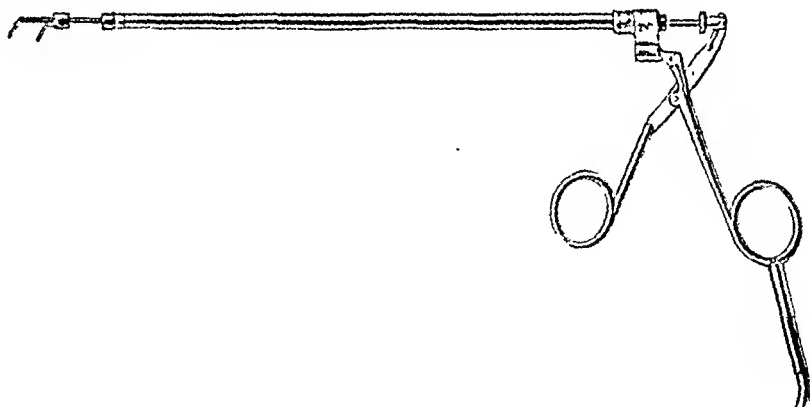


Fig. 1.—Lateral view of instrument.

The shaft with the loops has a rotating mechanism near the handle which permits rotation of 360 degrees, akin to that I have already described.¹ Thus, by rotating the shaft of the instrument, the loops can be made to face a suspected lesion located anywhere on the circumference of the terminal towel.

Since the loops are constructed of wire, they offer no appreciable obstruction to vision and thus the lesion remains in full view during

¹Received for publication, Jan. 8, 1942.

18. Lockhart-Mummery, J. P.: *Diseases of the Rectum and Colon and Their Surgical Treatment*, Baltimore, 1934, William Wood & Company, 605 pp.
19. MacFec, W. F.: Resection With Aseptic End-to-End Anastomosis for Carcinoma of the Colon, *Ann. Surg.* 106: 701-714, 1937.
20. Magill, W. S.: Resection of the Ileo-rectal Coil of the Intestine; Its Indications, Results, and Modus Operandi, With a Review of One Hundred Two Reported Cases and Two Heretofore Unpublished, *Ann. Surg.* 20: 642-675, 1894.
21. Mayo, C. W., and Lovelace, W. R., II: *Malignant Lesions of the Cecum and Ascending Colon*, Tr. West. S. A. pp. 378-421, 1939.
22. Mikulicz, Joh: *Small Contributions to the Surgery of the Intestinal Tract*, 4. On Operation on Malignant Growths of the Large Intestine, Tr. Am. S. A. 21: 132-134, 1903.
23. Moynihan, Berkeley: *Abdominal Operation*, ed. 4, Philadelphia, 1926, W. B. Saunders Company, 642 pp.
24. Patterson, Howard, and Webb, Alexander, Jr.: The Mikulicz Procedure With Special Reference to Late Results in Management of Carcinoma of the Colon, *Ann. Surg.* 111: 64-75, 1940.
25. Paul, F. T.: Colectomy, *Brit. M. J.* 1: 1136-1139, 1895.
26. Pemberton, J. deJ., and Whittaker, L. D.: Resection of the Right Half of the Colon, *Surg., Gynec. & Obst.* 65: 92-99, 1937.
27. Pilcher, L. S.: Use of Potato Bobbin to Facilitate Enterorrhaphy; Carcinoma of the Splenic Flexure of the Colon, *Ann. Surg.* 25: 485-486, 1897.
28. Rankin, F. W.: *The Principles of Surgery of the Colon*, *Surg., Gynec. & Obst.* 72: 332-340, 1941.
29. Rankin, F. W., Bergen, J. A., and Buie, L. A.: *The Colon, Rectum and Anus*, Philadelphia, 1932, W. B. Saunders Company, 846 pp.
30. Ransom, H. K.: Carcinoma of the Right Colon, *SURGERY* 5: 340-357, 1939.
31. Sistrunk, W. E.: The Mikulicz Operation for Resection of the Colon: Its Advantages and Dangers, *Ann. Surg.* 88: 597-606, 1928.
32. Starr, F. N. G.: Resection of the Cecum, *Ann. Surg.* 94: 610-611, 1931.
33. Stone, H. B., and McLanahan, Samuel: *Surgical Aspects of Carcinoma of the Large Bowel*, J. A. M. A. 113: 2282-2286, 1939.
34. Wakeley, C. P. G., and Rutherford, R.: Carcinoma of the Cæcum; a Discussion of Its Incidence, Diagnosis and Treatment With a Report of Twenty-five Personal Cases, *Brit. J. Surg.* 20: 91-112, 1932.
35. Wangensteen, O. H.: Aseptic Resections in the Gastro-intestinal Tract With Special Reference to Resection of the Stomach and Colon, *Surg., Gynec. & Obst.* 72: 257-281, 1941.
36. Wilkie, David: *Surgery of Malignant Disease of the Colon*, Edinburgh M. J. 46: 1-16, 1939.

METHOD OF CLOSING THE PYLORO-ANTRAL POUCH IN THE ANTRAL EXCLUSION OPERATION*

OWEN H. WANGENSTEEN, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

FINSTERER, described antral exclusion as an alternative method of dealing with the difficult, indurated ulcer during the course of gastric resection for duodenal ulcer. In the same paper, Finsterer stated that the mucosa from the residual antral fragment might be removed at the same time. As recently as 1934, however, Finsterer insisted that it did not make any appreciable difference in the end result, whether the antral mucosa was removed or allowed to remain. At that time, he stressed extending the resection proximally, removing usually two-thirds of the stomach; also, he believed it important to attempt to obviate retrograde filling of the afferent jejunal loop of the gastrojejunal stoma. In 1934, Finsterer admitted an incidence of gastrojejunal ulcer in 6.4 per cent of the patients upon whom he had performed the antral exclusion operation. In the meantime (1940), apparently, Finsterer has adhered more consistently to the more extensive gastric resection and has become alert to the great importance of excising the mucosa from the residual antral pouch, even though he allows the pyloric sphincter to remain. With this practice, Finsterer has not observed the occurrence of gastrojejunal ulcer following the antral exclusion operation.

In 1926, the Dutch surgeon, Wilmanns, pointed out the importance of excision of the antral mucosa for the success of the antral exclusion operation for duodenal ulcer. Wilmanns stated that he had performed antral exclusion with simultaneous removal of the antral mucosa in difficult duodenal ulcers since 1923. He divided the antrum 2 cm. proximal to the pylorus and dissected out the antral cylinder of mucosa and closed the resulting seromuscular pouch. In 1931, Drüner, in a very brief paper, composed of two short paragraphs, mentions that he had performed such an operation, not unlike that described previously by Wilmanns. Independently, Baneroff (1932), in this country, described excision of the antral mucosa as a variant of the Devine exclusion operation for duodenal ulcer. In the preceding three and a half years, Baneroff had done fourteen such operations, all the patients making a satisfactory operative recovery. Baneroff states that he was led

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resection. The light construction of the loops is made possible by the apparent absence of resistance of the tissues to the cutting current.

To remove a tumor, the open loops are placed upon the neoplasm; the desired cutting current is applied and the loops are closed as illustrated in Fig. 2. These maneuvers are repeated until all the intraluminal

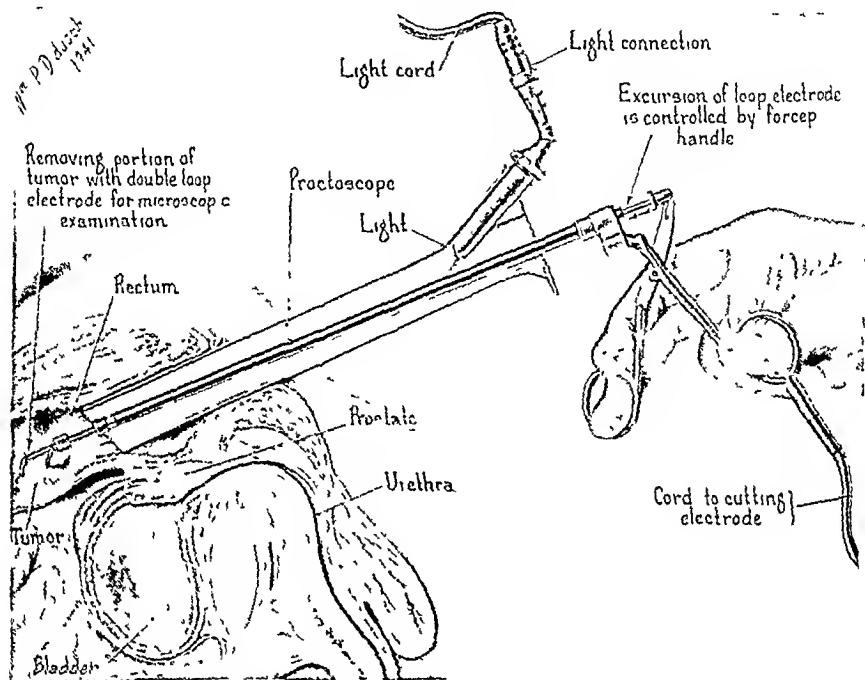


Fig. 2—Sagittal section showing removal of portion of tumor, note the travel of the proximal active electrode.

projections of the neoplasm are resected; the base of the tumor may be coagulated at the conclusion of the resection or at a later date. Bleeding is usually prevented by the hemostatic effect of the cutting current or it may be easily controlled by coagulation (with the same instrument) merely by substituting the coagulating for the cutting current.

I am indebted to Mr. F. C. Wappler and Mr. H. S. Rubens of the American Cystoscope Makers, Inc., New York, N. Y., for their technical advice, and to Mr. W. P. Didusch for the illustrations.

REFERENCE

1. Turell, R.: A New Recto Sigmoidal Biopsy Forceps, *Ann. Surg.* (To be published.)

who admits a higher incidence of postoperative complications with the exclusion operation. Finsterer admits, too, that he finds it necessary to employ drainage quite frequently.

THE EXPERIENCE OF THIS CLINIC WITH THE ANTRAL EXCLUSION OPERATION

Somewhat more than four years ago, a plan was set up in this clinic to test the capacity of a number of operations for ulcer to reduce gastric acidity. As others (Ogilvie, 1938, and Allen and Welch, 1942), we learned, too,¹⁹ to our sorrow, that antral exclusion without exenteration of the antral mucosa, even though accompanied by extensive gastric resection, was a poor operation for ulcer, in that it failed to protect the patient against gastrojejunal ulcer. When, however, excision of the antral mucosa was added (described as the 4a operation in this clinic, see Fig. 1), this procedure appeared to be equally as effective as the Group 3 operation (extensive gastric resection with excision of pylorus and antrum) in depressing effectively the secretion of hydrochloric

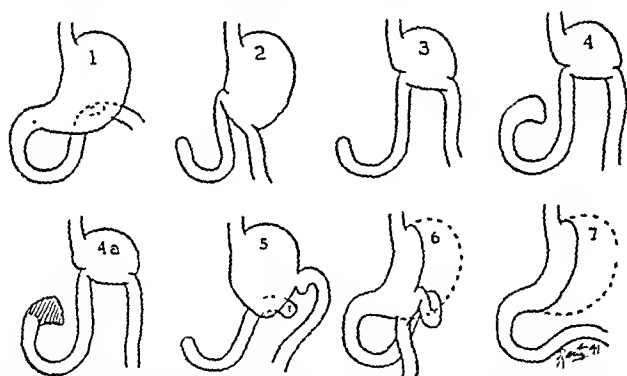


Fig 1—Types of operation subjected to scrutiny in this clinic. Fairly consistent achlorhydria attends only operations 3, and 4a (Arch. Surg. 44: 48, 1942)

acid and in ridding the patient of the ulcer diathesis. As a matter of fact, not a single stomal ulcer has attended either the Group 3 or 4a operation in this clinic. However, we experienced the same difficulties with the technical features of the 4a operation (antral exclusion and excision of antral mucosa) that Allen (1942) and Allen and Welch (1942) described. The first operation of this type was performed in this clinic in January, 1941. By August, 1941, thirteen such operations had been performed. Of this number, two developed a subphrenic abscess, necessitating surgical drainage (C. K., University Hospital No. 705300 and G. B., University Hospital No. 706376). In the instance of the latter patient, a drain had been placed beside the antral inversion. In both patients, the abscess formed beneath the left diaphragm, an occurrence emphasized previously by Carter. In two additional patients, the nature of the antral closure was such as to suggest the necessity for the employment of drainage. All the patients in the group recovered.

to perform excision of the antral mucosa as an adjunct to the Devine exclusion operation on the suggestion of Dr. L. G. Cole, who believed that removal of the antral mucosa would improve the results of the Devine operation. Baneroff's illustrations suggest that he removed the mucosa from about the distal one-third of the stomach, certainly from the entire antrum. He did not then recommend simultaneous resection of the corporic and fundic zones (actively secreting) of the gastric mucosa, as had Finsterer (1918) and Wilmanns (1926) previously.

In the intervening years, antral exclusion with excision of the antral mucosa, as an item in the operation of extensive gastric resection for duodenal ulcer, has gained in popularity among gastric surgeons. Edkins (1904) had pointed out, many years before that, the antral mucosa, although it did not itself secrete hydrochloric acid, augmented the secretion of hydrochloric acid from the corporic and fundic zones of the gastric mucosa. The operation of antral exclusion with excision of the antral mucosa, therefore, has a sound physiologic basis. The Edkins' hypothesis of hormonal control of the gastric phase of gastric secretion is probably correct only in part, for as has been pointed out previously,^{13, 18, 19} the small gastric resection with complete removal of the antrum will fail to protect a patient from recurrent ulcer unless an accompanying extensive resection of the corporic and fundic portions of the stomach is done simultaneously.

In Germany, Bürkle-de la Camp (1933) and Plenck (1936) expressed enthusiasm over the antral exclusion operation and depicted technical features of the operation. Zukschwerdt and Horstmann (1936) named a number of German surgeons who had displayed an interest in the procedure.

The experience of Ogilvie (1938) with the antral exclusion operation has served to focus important notice on excision of the antral mucosa for the success of gastric resection for duodenal ulcer. It is now a matter of common experience among surgeons that leaving a small fragment of antral gastric mucous membrane may prejudice the result, even though extensive simultaneous excision of the corporic and fundic (actively secreting) mucosa is made. Two such patients have been observed in this clinic.¹⁰

Allen (1942) and Allen and Welch (1942) endorse the operation of antral exclusion with excision of the antral mucosa for difficult duodenal ulcers, when accompanied by simultaneous extensive gastric resection. They report thirteen instances in which the operation was done, with one death. They point out that, whereas the end results of this operative procedure parallel closely the splendid achievement of the more extensive operation in which pyloric sphincter and antrum are removed completely, the incidence of complications is greater and the postoperative convalescence may be considerably longer in the antral exclusion group. This experience parallels that of Finsterer (1940),

who admits a higher incidence of postoperative complications with the exclusion operation. Finsterer admits, too, that he finds it necessary to employ drainage quite frequently.

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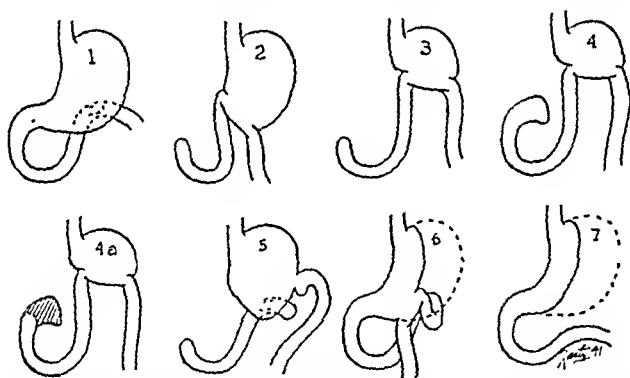


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Inasmuch as our experience with duodenal closure in the Group 3 operation, whether done for gastric ulcer, cancer, or duodenal ulcer had been eminently satisfactory, it was obvious that the difficulty lay with the nature of the closure. In the first group, the closure was effected as shown in Fig. 2. Since then,¹² fifteen additional antral exclusions with simultaneous excision of the antral mucosa have been done as an incident in extensive gastric resection for indurated duodenal ulcer according to the plan shown in Fig. 3.

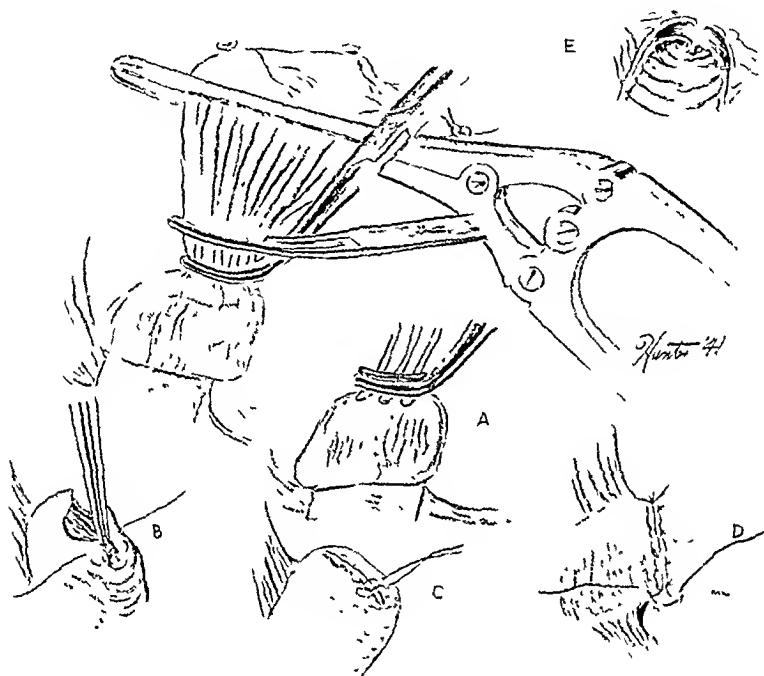


Fig. 2.—Technique of the antral exclusion operation as employed in the first series of cases; the procedure illustrated here probably conforms to standard surgical practice. The mucosa is clamped and divided at the pylorus. In A is illustrated the closure of the divided pyloric mucosa, which may be done with a running suture of catgut just as well. In B, C, and D are illustrated the technique of securing closure of the remaining seromuscular antral pouch by two inversion sutures as a matter of fact, the matter is not as simple as illustrated here (see text), for the antral funnel narrows toward the pylorus. In E is shown another cause for failure of this type of operation, namely, persistence of a closed space. These two items, difficulty of inversion, and dead space make the usual method of closure of the pyloro-antral pouch unsatisfactory.

TECHNIQUE

The only essential difference in these two techniques of performing the antral exclusion operation relates to the manner of effecting closure of the resultant antral pocket denuded of antral mucosa. In both procedures, the mucosa at the pyloric valve was divided and closed with a running suture of catgut in an identical manner. In the earlier operations, closure of the residual antral pocket was accomplished by one or two inverting rows of interrupted silk sutures. Inasmuch, however,

as the remaining antral pouch narrows toward the pylorus like a funnel, it is obvious that satisfactory inversion of the peritoneal margins of the rim of the antral funnel may be very difficult and even impossible of nice and precise accomplishment without tension on the sutures. Another weakness of the inversion method of closure lies in the leaving of a dead space (Fig. 2E), an item to which Baneroff (1932) and Plenck (1936) had drawn attention; if this dead space is obliterated by sutures from within the pouch, the inversion, in turn, is made even more difficult. Finsterer (1940) employs two rows of inversion sutures to secure closure of the antral pouch after excision of the mucous membrane. Baneroff (1942) states that he has latterly employed triple inversion.

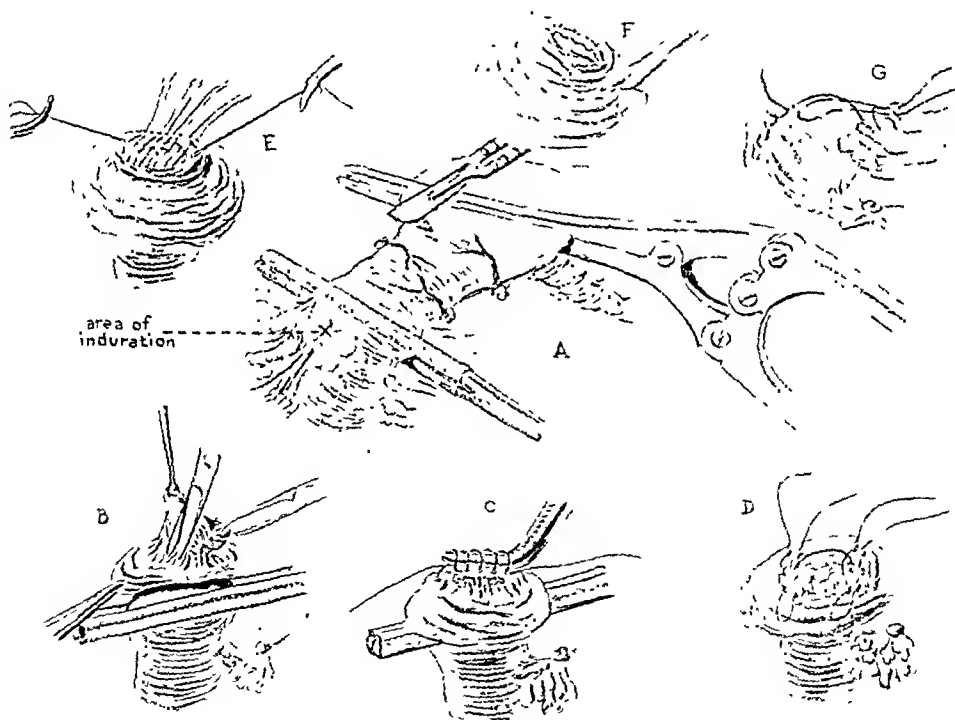


Fig. 3.—Technique of closure of the pyloro-antral pouch described herein and now in current use at the University Hospitals. A, Division of the antrum 4 to 5 cm. above the pylorus (usually slightly less than 4 cm.); a rubber-shod clamp just below the pylorus provides secure retraction. B, Dissection and the devascularization is carried up to the area of induration. C, Closure of the divided pyloric mucosa by two 3-0 silk sutures. D, Approximation of the circular muscle by a half purse string. E, The circular muscle, to be approximated by Halsted mattress sutures of fine silk, is well shown here. F, The suture completed. Two rows of Halsted sutures may be placed; the dotted line indicates the site for excision of the superfluous seromuscular pouch. The rubber-shod clamp is removed at this part of the operation. G, The trimmed edges of the pouch have been approximated without inversion. (Interrupted Halsted mattress sutures of fine silk or a simple running stitch of catgut; finally, as shown here, the closure is capped with omentum or a margin of the right border of the transverse mesocolon.)

The difficulties related above suggested that the peritoneal inversion should be omitted altogether. During the past year (since August, 1941), the antral exclusion operation has been performed as shown in Fig. 3. The mainstay of this procedure, which, in our hands, has been uniformly successful, lies in a careful approximation of the submucous and circular muscle layers by a single row of interrupted sutures of fine silk, placed after the Halsted mattress pattern, immediately above the closure of the pyloric mucous membrane. In the lower portion of the antral pocket near the pylorus, the circular fibers of the muscle coat of the antrum stand out very prominently (Fig. 4), and appear, when

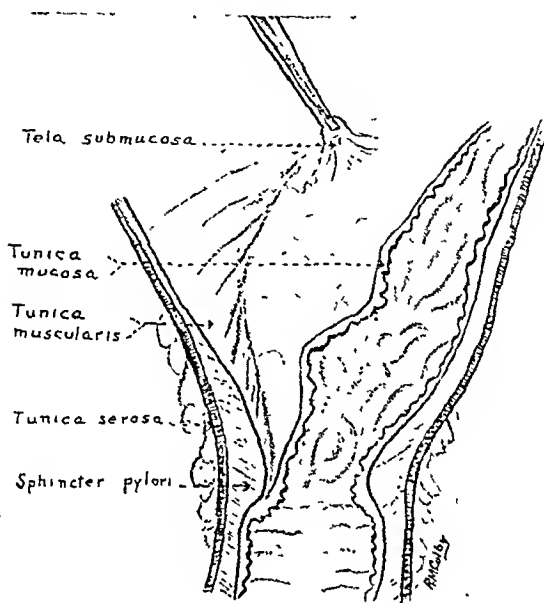


Fig. 4.—Drawing from a post-mortem specimen. A 10 per cent formalin solution was put into the stomach at autopsy, the duodenum and esophagus being ligated; after forty-eight hours of refrigeration this dissection was made. It is to be noted that the circular muscle is a well-developed muscle several centimeters proximal to the pyloric sphincter. This observation is well known to anatomists. It is approximation of these circular muscle fibers that is important in effecting an adequate and safe closure of the pyloro-antral pouch. Microscopic studies of the antral mucosa removed at operation indicate that the submucosa is removed with the mucosa.

viewed from the inside of the residual antral pouch, not unlike a sphincter muscle which, in fact, this circular muscle becomes at the pylorus. After placement of a row of interrupted silk sutures, the remnants of the pouch are cut away, leaving only enough tissue to permit easy approximation of the edges, *without inversion*. If the circular muscle of the pouch is particularly well developed, a second row of interrupted silk sutures may be placed, if it is felt desirable. The final approximation of the edges of the peritoneal muscular cuff may be made with running catgut or a few silk sutures. As a final gesture, the closed pouch is covered with a wisp of omentum or it may be buried

gently in the extreme right portion of the right transverse mesocolon. Drainage is not employed.

Ordinarily, patients in our clinic are dismissed from the hospital on the eleventh day after gastric resection. In this latter group of antral exclusion operations, only one patient stayed longer. This patient developed a prostatitis from an indwelling urethral catheter (the only complication in the series), necessitating a postoperative hospital stay of twenty days.

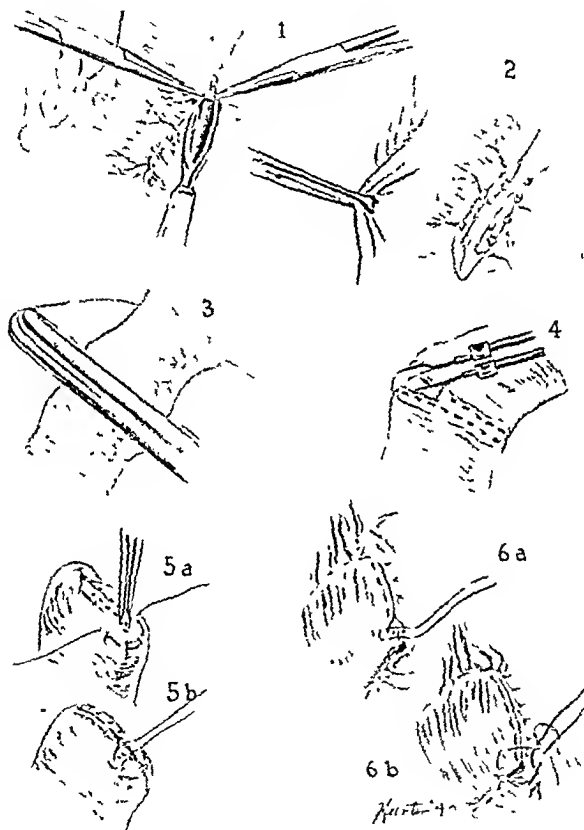


Fig 5A

Fig 5—A and B, Methods in use in this clinic for performance of the Group 3 operation in which antrum and pylorus are excised. A, The method of election for closure of the duodenum. 1 to 6 indicate the various steps in the procedure. (Reproduced from *SUPPEY* 8: 275, 1910 and *Surg., Gynec. & Obst.* 72: 260, 1941.)

INDICATIONS FOR THE ANTRAL EXCLUSION OPERATION

The only justification for this procedure lies in the rather frequent occurrence of an indurated duodenal ulcer; under these circumstances it is difficult to mobilize the duodenum and obtain a secure closure. During the past year, it has been observed in this clinic that such ulcers have not infrequently an antecedent story of obstruction. From our

experience it would appear that an occult, sealed duodenal perforation is the most common cause of pyloric obstruction by duodenal ulcer.²⁰ Duodenal stenosis, in our experience, is a rather uncommon occurrence. An ulcer in the pyloric valve may cause obstruction without actual penetration of the entire wall. This occurrence too, however, is far less commonly a cause of obstruction than the sealed occult duodenal perforation. The area of induration in juxtaposition to the ulcer crater apparently brings about extrinsic duodenal compression and obstruction.

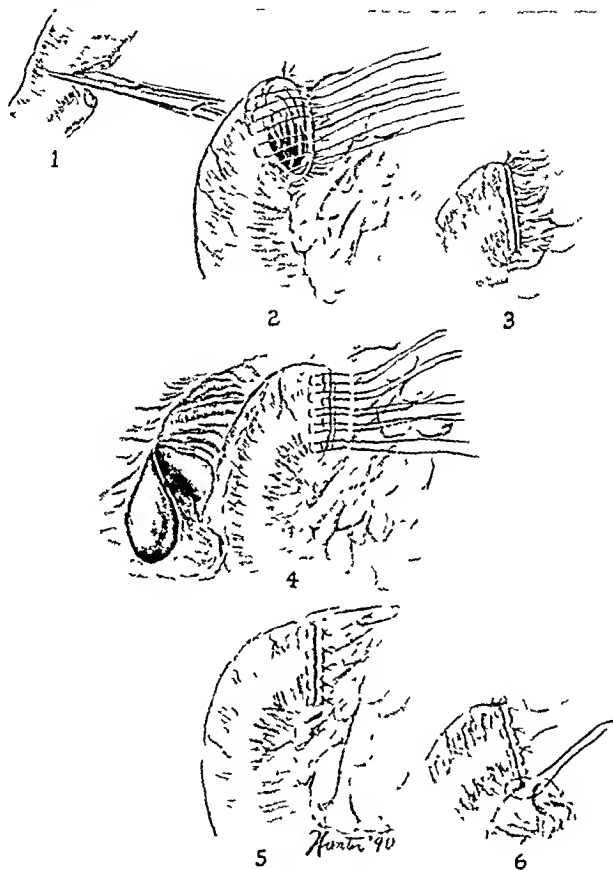


FIG 5B

Fig. 5B.—The method employed for a sealed posterior duodenal perforation in the presence of active hemorrhage, or when the perforation is broken into during the course of the dissection.

It is this type of case in which the antral exclusion operation is indicated. Whereas a posterior duodenal perforation may be dealt with ordinarily with no great difficulty by the technique shown in Fig. 5B, a sealed duodenal perforation (at the gastroduodeno hepatic ligament) is usually very difficult to close effectively by any means (Fig. 6). The area of induration in juxta-

position to the ulcer crater robs the surgeon of readily available tissue to utilize in the closure. Yet, even these ulcers may be closed when the surgeon encounters this situation in an actively bleeding duodenal ulcer; under these circumstances he is forced to uncover the bleeding point. In the patient, with a bleeding duodenal ulcer, operated upon after the risk of active hemorrhage has passed, the antral exclusion operation may be considered to be the operative procedure of choice. If the surgeon fails to suppress his curiosity over the nature of the ulcer crater and pursues his dissection until he ascertains its exact nature, he may become ensnared in a trap by the supraduodenal ulcer perforation. This meddlesome venturesomeness of the surgeon may cost him hours of tedious effort to extricate himself and his patient from the difficulty. It is for this type of duodenal ulcer that the antral exclusion operation is ideal. It saves the surgeon much labor and grief.

Obviously, the antral exclusion operation is not intended for a perforated prepyloric ulcer. In order to insure maximal protection against ulcer recurrence, *all* of the antral mucosa *must* be excised.

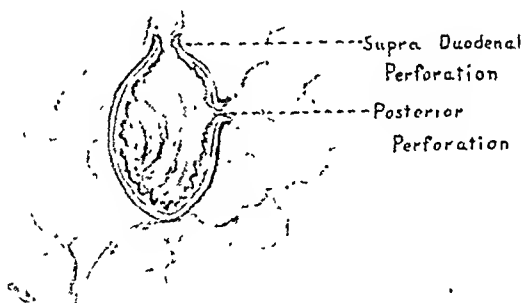


Fig. 6.—Schematic drawing which give rise to the necessity excision of antral mucosa; it is difficult to close and for which it

non sites of sealed perforation antral exclusion operation with perforation which is particularly herein is particularly adapted.

Allen and Welch (1942) state that "McKittrick has suggested a deliberate two-stage resection in poor risk patients who have extensive ulceration or inflammatory reaction." Finsterer (1940), too, employs the two-stage antral exclusion operation in patients who have both duodenal ulcer and cholelithiasis. In this clinic, the one-stage gastric resection is done regularly, the patient, if obstructed, being prepared by intragastric drip feedings of a mixture rich in carbohydrate and protein and low in fat (Varco, gastric diet No. 2),¹⁷ or by intravenous feedings if the pyloric obstruction does not relent. Simultaneous excision of a diseased gall bladder encountered coincidentally during gas-

experience it would appear that an occult, sealed duodenal perforation is the most common cause of pyloric obstruction by duodenal ulcer.²⁰ Duodenal stenosis, in our experience, is a rather uncommon occurrence. An ulcer in the pyloric valve may cause obstruction without actual penetration of the entire wall. This occurrence too, however, is far less commonly a cause of obstruction than the sealed occult duodenal perforation. The area of induration in juxtaposition to the ulcer crater apparently brings about extrinsic duodenal compression and obstruction.

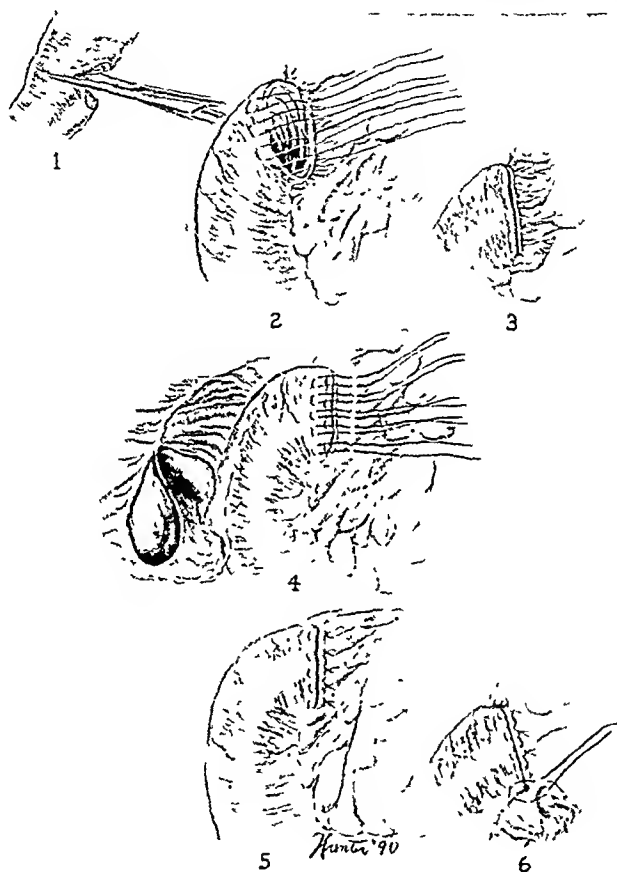


Fig. 5B.

Fig. 5B.—The method employed for a sealed posterior duodenal perforation in the presence of active hemorrhage, or when the perforation is broken into during the course of the dissection.

It is this type of case in which the antral exclusion operation is indicated. Whereas a posterior duodenal perforation may be dealt with ordinarily with no great difficulty by the technique shown in Fig. 5B, a sealed duodenal perforation at the superior margin of the duodenum (at the gastroduodeno hepatic ligament) is usually very difficult to close effectively by any means (Fig. 6). The area of induration in juxta-

11. Finsterer, H.: Die Bedeutung der Resektion zur Ausschaltung für die unmittelbaren Operationserfolge und die Fernresultate der operativen Behandlung des Uleus duodeni, *Zentralbl. f. Chir.* 67: 610, 1940.
12. Hay, L. J., Varco, R. L., Code, C. F., and Wangensteen, O. H.: The Experimental Production of Gastric and Duodenal Ulcers in Laboratory Animals by the Intramuscular Injection of Histamine in Beeswax, *Surg., Gynec. & Obst.* 75: 170, 1942.
13. Lannin, B. G.: Evaluation of Surgical Attempts at Reduction of Gastric Acidity, Unpublished Master's Thesis.
14. Ogilvie, W. H.: Physiology and the Surgeon, *Edinburgh M. J.* 43: 61, 1936.
15. Ogilvie, W. H.: Approach to Gastric Surgery: II. Ulcer of the Stomach, *Lancet* 2: 295, 1938.
16. Plenk, A.: Zur Technik der Resektion zur Ausschaltung, *Zentralbl. f. Chir.* 63: 3019, 1936.
17. Varco, R. L.: Unpublished data.
18. Wangensteen, O. H.: The Surgeon and the Ulcer Problem: With Emphasis on (1) Definition of the Criteria of an Acceptable Operation and (2) the Importance of Maintaining Caloric and Nitrogen Balance in the Preoperative Preparation and the Recovery Period in Poor Risk Patients, *Illinois M. J.* 80: 100, 1941.
19. Wangensteen, O. H., and Lannin, B. G.: Criteria of an Acceptable Operation for Ulcer: The Importance of the Acid Factor, *Arch. Surg.* 44: 489, 1942.
20. Wangensteen, O. H.: Unpublished data, 1942.
21. Wangensteen, O. H., Varco, R. L., Hay, L. J., Walpole, S. H., and Trach, B.: Gastric Acidity Before and After Operative Procedure With Special Reference to the Role of the Pylorus and Antrum: A Preliminary Report of a Clinical and Experimental Study, *Ann. Surg.* 112: 626, 1940.
22. Wilmanns, R.: Resectio praepylorica bei uleus duodeni, *Zentralbl. f. Chir.* 53: 1874, 1926.
23. Zuckschwerdt, L., and Horstmann, H.: Die operative Behandlung des nicht oder schwer resezierbaren peptischen Geschwürs. Berechtigung und Anwendung der palliativen Resektionsmethoden für das Uleus duodeni (Finsterer), das hochsitzende Geschwür (Madlener) das Uleus pepticum jejuni (Kreuter), *Ergebn. d. Chir. u. Orthop.* 29: 440, 1936.

tric resection for ulcer or carcinoma has been performed a number of times in this clinic. As yet, no suggestion has been observed that such an additional procedure enhances the risk. Obviously, the surgeon must be willing to take enough time to do the incidental procedure as well as the one for which operation was undertaken primarily. Our practice has been to attempt to prepare the patient well for one operation and to take enough time to do it to the surgeon's complete satisfaction. The experience of this clinic suggests definitely that the necessity of operating quickly is only a myth, granted satisfactory preoperative preparation of the patient and well-controlled management of the patient during and after operation.

SUMMARY AND CONCLUSIONS

The success of the antral exclusion operation when combined with simultaneous extensive gastric resection suggests that: (1) The pyloric sphincter need not be excised to effect a cure of ulcer; (2) the duodenal ulcer may be left and the ulcer diathesis done away with; it is not the ulcer itself which constitutes the real hazard for the patient with an ulcer, but the acid ulcer diathesis. Extensive gastric resection, when accompanied by complete excision of the antral mucosa, abolishes the ulcer diathesis.

The antral exclusion operation with sacrifice of all of the antral mucosa when accompanied by an extensive gastric resection is a satisfactory and effective operation for so-called irremovable or inoperable duodenal ulcer. The operation has not come into general favor among gastric surgeons because of the likelihood of leakage from the residual antral pocket. A technique of performing the antral exclusion operation, with excision of the antral mucosa in which leakage can be avoided, is described.

REFERENCES

1. Allen, A. W.: Surgical Treatment of Duodenal Ulcer, Arch. Surg. 44: 501, 1942.
2. Allen, A. W., and Welch, C. E.: Gastric Resection for Duodenal Ulcer: Follow-up Studies, Ann. Surg. 115: 530, 1942.
3. Bancroft, F. W.: A Modification of the Devine Operation of Pyloric Exclusion for Duodenal Ulcer, Am. J. Surg. 16: 223, 1932.
4. Bancroft, F. W.: Discussion of paper by Allen and Welch, 1942.
5. Bürkle-de la Camp, H.: Beitrag zur Resektion zur Ausschaltung, Deutsche Ztschr. f. Chir. 240: 456, 1933.
6. Carter, B. N.: Left Subphrenic Abscess, Ann. Surg. 110: 562, 1939.
7. Drüner, L.: Über die Exstirpation der Schleimhaut des peripheren Magens stumpfes bei unausführbarem Billroth II, Zentralbl. f. Chir. 58: 1510, 1931.
8. Edkins, J. S.: The Chemical Mechanism of Gastric Secretion, J. Physiol. 34: 133, 1906.
9. Finsterer, H.: Ausgedehnte Magenresektion bei Ulcus duodeni statt der einfachen Duodenalresektion bzw. Pylorusausschaltung. Zentralbl. f. Chir. 45: 434, 1918.
10. Finsterer, H.: Resektion zur Ausschaltung oder Gastro-Enterostomie beim nicht resezierbaren Ulcus duodeni. Zentralbl. f. Chir. 61: 1624, 1924.

and trachea. Postoperative tracheitis and edema of the larynx causing obstruction may be the likely consequences. When the trachea is very thin, it is difficult to see why perforation may not occur, though I have found no reported case.

Few intrathoracic goiters require the use of an intratracheal catheter for their removal. The decision as to its necessity generally cannot be made prior to operation. In the presence of tracheal obstruction local anesthesia alone should be used at least until the trachea has been exposed. After exposure of the trachea, should an intratracheal catheter be considered necessary, it may be inserted through a tracheotomy and the operation continued under local or general anesthesia, or the catheter may be passed transorally in which case general anesthesia would be instituted. The technique of the removal of an intrathoracic goiter is materially affected by whether or not an intratracheal catheter is used. Without a catheter in place, local anesthesia is generally used. Extreme gentleness is of the utmost importance. Operative manipulation must guard against increased pressure upon the trachea and, if possible, steadily relieve the pressure already upon it. In case the obstruction is at the superior strait, the airway often improves sufficiently during the course of the operation to permit the institution of inhalation anesthesia. The use of the intratracheal catheter is usually attended by general anesthesia, particularly if the transoral route is used. The trachea is protected against obstruction and the patient is unconscious of pain, thus permitting a more rapid performance of the operation.

It is my practice to use the intratracheal catheter not as a routine procedure of choice but only when indications for its need develop during the course of the operation. The catheter is then passed through a tracheotomy tube. The management of these cases in this manner will be considered.

Absolutely essential is proper preoperative preparation. Upon admission to the hospital these patients often maintain an adequate air exchange only with a conscious effort. Sleep brought on by exhaustion is soon interrupted by periods of respiratory obstruction likely caused by change in the position of the head. Coughing paroxysms are frequent and often appear alarming. They are generally caused by attempts to bring up accumulations of mucus that may collect below the obstruction. One patient was observed to bring up long casts of the trachea and bronchi, which she would extract with her fingers.

In most instances the pressure symptoms are greatly relieved by bed rest and the use of opiates and other sedatives. The cough practically subsides, the excess mucus ceases to form and breathing becomes easier. Hyperthyroidism, if present, must be taken into proper account. The usual preoperative treatment requires from one to several weeks.

The position of the patient on the operating table must be such as to permit an adequate air exchange, without undue effort. This is often

OPERATIVE TECHNIQUE FOR INTRATHORACIC GOITER WITH ESPECIAL REFERENCE TO THE MAINTENANCE OF AN AIRWAY

WILLIAM H. PRIOLEAU, M.D., F.A.C.S., CHARLESTON, S. C.

(From the Department of Surgery, Medical College of the State of South Carolina)

ONE of the chief difficulties in the removal of an intrathoracic goiter is the maintenance of an adequate airway. While an intratracheal catheter inserted immediately before the operation accomplishes this, its use is attended by certain difficulties and dangers. Its introduction may be hindered by such conditions as displacement of the larynx, spasm of the vocal cords, and narrowing and angulation of the trachea. Extension of the neck for the purpose of passing the catheter may not be tolerated by the patient because of obstruction to breathing. These difficulties may be overcome in part by local anesthesia of the larynx and a skillful anesthetist.

In the presence of tracheal obstruction, general anesthesia cannot be relied upon for the introduction of the catheter. Inhalation anesthesia may provoke spasm of the larynx. Also, a sufficient amount of the anesthetic agent may not pass the partially obstructed trachea. Rectal or intravenous anesthesia would avoid the foregoing objections, but still are not suitable, as patients with an inadequate airway do not maintain a sufficient air exchange under general anesthesia, a conscious effort apparently being necessary. Contrary to the above, Lahey³ reports that sufficient depth of anesthesia and relaxation for the passage of the intratracheal catheter generally can be obtained by inhalation of a mixture of oxygen, cyclopropane, and helium. Helium, due to its low specific gravity, acts as a diluent of the oxygen and permits it to pass more readily by the obstruction. Sise⁴ later reports this to be effective in only the mildest cases of obstruction.

Regardless of the anesthesia employed, an unsuccessful attempt to insert an intratracheal catheter may result in a complete obstruction to respiration, necessitating a tracheotomy under most adverse conditions. If an intratracheal catheter is decided upon, it would appear safer to make a preliminary exposure of the trachea under local anesthesia, a procedure in itself not without difficulty in the presence of considerable overlying thyroid tissue.

While an intratracheal catheter protects the trachea against collapse by operative manipulation and thus facilitates the removal of the gland, its passage and presence may be attended by some trauma to the larynx

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is made over the midsternum. The sternum is bisected to the second or third interspace at which level it is divided to the indicated side and the incision continued in the intercostal space. This results in the formation of a sternoclavicular costal flap which can be retracted anterolaterally, greatly enlarging the superior strait. Even with this exposure, delivery of the goiter may be difficult if it is situated posteriorly to the large blood vessels. In such an operation local anesthesia ceases to be adequate beyond the cervical portion, particularly for the retraction of the chest wall flap; however, by this time there is generally sufficient airway to permit an inhalation anesthesia. Otherwise anesthesia can be administered through an intratracheal catheter passed through a cervical tracheotomy. This operation is followed by considerable pain in the shoulder and upper costovertebral region. Partial removal of the sternum by rongeur is held preferable by some.

Should a tracheotomy be necessary the tube should be inserted low through a horizontal incision between two rings. If no longer necessary at the end of the operation, the tube can be removed and the opening closed with pretracheal fascia.

By following this plan of management, unnecessary trauma to the trachea and the larynx by the intubating catheter is avoided by limiting its use to those cases in which it is necessary for the maintenance of an adequate airway. There is provided the safety factor of exposure of the trachea as a preliminary procedure in case intratracheal catheterization should become necessary. As the operation proceeds there is the tendency for a steady increase in the size of the airway except for the period during the delivery of the intrathoracic lobe. The constant care necessary to avoid pressure upon the trachea and the use of local anesthesia prolong the operation and make it more exacting upon the surgeon, but also add to its safety. The use of the intratracheal catheter during operation can be avoided to advantage in most cases of intrathoracic goiter and in nearly every case of tracheal obstruction due to external pressure in the neck, such as cervical goiter, malignancy, and abscess.

CASE 1 (Hospital No. 29459).—J. W. S., a white woman, aged 34 years, was admitted to the Roper Hospital, Oct. 14, 1938. She had first noticed the presence of a goiter four or five years previously. She had been advised by a physician that treatment was unnecessary as the basal metabolic rate was not elevated. During the past nine months the goiter had increased in size and she had symptoms from pressure upon the trachea. She complained of palpitation, nervousness, and emotional instability and had lost twenty pounds in weight.

The positive physical findings were nervousness, a staring expression, and tachycardia, all of a moderate degree. On both sides and in front of the trachea there was a large, firm, nodular mass of thyroid gland, extending well posteriorly and inferiorly. The basal metabolic rate was minus 11 per cent and the blood cholesterol 163 mg. per cent. X-ray examination showed a well-defined area of increased density extending several centimeters to the right of the trachea and situated well below the superior strait (Fig. 1).

The diagnosis was nodular goiter, cervical and intrathoracic with partial obstruction of the trachea, and mild hyperthyroidism.

an awkward position for the performance of the operation. Particular care must be taken not to excite the patient or cause undue pain, as struggling caused thereby will result in exhaustion and likely complete respiratory obstruction necessitating a tracheotomy under most unfavorable conditions.

Novocain is infiltrated into the operative field, first subcutaneously and then as the operation proceeds. A long horizontal incision is made through the skin and platysma a few centimeters above the clavicles. Upper and lower flaps are reflected. The prethyroid muscles are divided in the midline from the thyroid cartilage to the sternum and then divided transversely on one or both sides as indicated.

Bleeding points must be ligated as encountered so as not to place the weight of the instruments upon the trachea and also to keep the operative field clear in case a tracheotomy becomes necessary. All manipulations must avoid pressure upon the trachea.

The trachea should now be well exposed. This may be done by proceeding between lobes or nodules. Often it is necessary to divide the overlying thyroid tissue. Once the trachea has been exposed the operator feels that he has control of the situation as he can safely make an opening for the insertion of a tube in case of obstruction to breathing. Before this a tracheotomy can be performed only with difficulty and danger, due to almost uncontrollable bleeding in a patient struggling for air. Should general anesthesia be necessary, only now can it be instituted without undue risk, particularly is this the case in the presence of obstruction.

The operation now proceeds along lines of least resistance freeing the upper pole, the lateral veins, and the tracheal attachments in order of easiest approach. It is important that all cervical attachments^{1, 2} be severed before attempting to deliver the mass from within the thorax. The one exception is the inferior thyroid artery which generally cannot be exposed without manipulating the gland so as to obstruct the trachea. The lobe is then firmly grasped with forceps, freed from its thoracic attachments by finger dissection, and delivered. During the act of delivery there may be obstruction of the trachea which is permissible for only a few seconds at a time. The lower pole is now cared for in the usual manner with due care to avoid injury to the recurrent laryngeal nerve. The preliminary removal of the contralateral cervical lobe is sometimes of advantage in affording more room. Drainage is generally advisable due to the tendency of fluid to collect in the space from which the goiter has been removed.

A lobe too large to be delivered intact may often be successfully removed by incising³ its capsule and breaking down its contents with the finger, thus reducing its size. An intrathoracic goiter occasionally is of such size, position, and fixation that it cannot be removed through an intact superior strait. In such cases a mediastinotomy becomes necessary. The cervical approach is made as described. A counter incision

CASE 2 (Hospital No. 31948).—J. T. H., a white woman, aged 55 years, was admitted to the Roper Hospital, Feb. 11, 1940. She had known of the presence of a goiter since the age of 16 years. There had been a gradual increase in its size. Lately she had been conscious of pressure in her neck causing difficulty in breathing, which was very pronounced at times. She had attacks of strangling in her sleep.

Physical examination revealed a large nodular mass of thyroid tissue on each side of the trachea, the right being larger than the left. The basal metabolic rate was plus 12 per cent, the blood cholesterol 167 mg. per cent. X-ray examination showed a moderate widening of the upper mediastinum which overshadowed most of the apex of the lung on each side (Fig. 2).

The diagnosis was nodular cervical and intrathoracic goiter with partial obstruction of the trachea.



Fig. 2 (Case 2, J.T.H.).—Intrathoracic goiter before operation.

On Feb. 15, 1940, operation was performed under local infiltration of novocain. A low collar incision was made through the skin. Flaps were reflected. An incision was made between the prethyroid muscles to the thyroid gland. Dissection was carried between the right lobe and the isthmus so as to expose the trachea. The isthmus was removed. The right lobe was the more accessible and thus resected first. This was done by freeing the tracheal attachments, the upper pole, and the lateral veins. The intrathoracic portion was then easily delivered and the lower pole severed. As the left lobe was much larger and of difficult approach, the prethyroid muscles were divided transversely. The trachea and larynx were displaced far to the right. The left lobe was mobilized by severing the tracheal attachments, the upper pole, and the lateral veins, in the order named. The intrathoracic portion was freed by finger dissection and then delivered with some difficulty, causing momentary obstruction to the trachea. The lower pole was severed and the lobe resected, leaving a small strip of tissue posteriorly. Black silk was used for hemostasis. A rubber tissue drain was placed on each side of the trachea and the wound closed. The convalescence was uneventful.

Pathologic Report.—The specimen consisted of two nodular masses of thyroid gland with a combined weight of 125 Gm. On section the tissue was reddish brown and showed circumscribed areas of cystic degeneration, colloid accumulation, and

On Oct. 21, 1938, operation was performed. Anesthesia was obtained by local infiltration of novocain. A low collar incision was made through the skin and flaps were reflected. A midline incision was made between the prethyroid muscles to the thyroid gland. The isthmus was divided and the trachea was exposed. A subtotal resection of the left lobe was made by freeing first the tracheal attachments, then the upper pole, the lateral veins, and finally the lower pole which extended well beneath the clavicle. The cervical portion of the right lobe was resected in a similar manner, being severed from the intrathoracic portion to which it was only slightly attached. The intrathoracic mass was grasped with forceps and freed by finger dissection; its size prevented its delivery. Its capsule was then incised and the contents broken down by digital manipulation, following which it was easily delivered and removed. A rubber tissue drain was placed on each side of the trachea and the wound was loosely closed. Thirty hours after operation there developed breathing difficulty and a fullness of the operative region. A deep hemorrhage was suspected and, accordingly, the wound was opened. A large blood clot was found to the right of the trachea. There was some oozing of bright red blood from the right lower pole, but no definite bleeding point was located. The wound was packed loosely with gauze. It was closed with drainage in twenty-four hours. The convalescence otherwise was smooth.

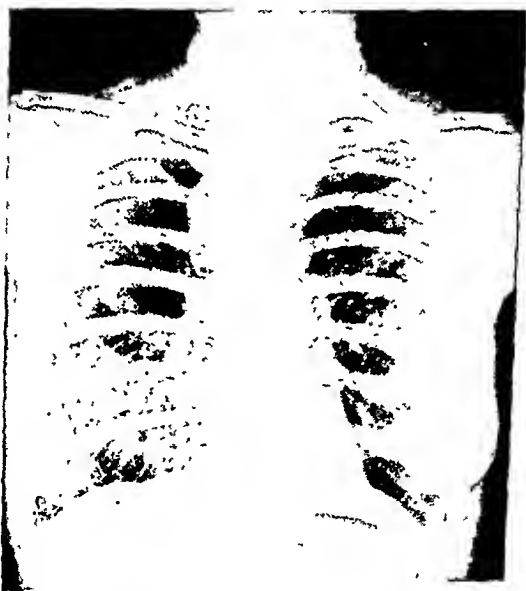


FIG. 1 (Case 1, J.W.S.).—Intrathoracic goiter before operation.

Pathologic Report.—The specimen consisted of three masses of nodular thyroid tissue, the largest being 6 by 5 by 2½ cm. Section revealed numerous nodular and cystic structures. Microscopic examination showed that in places the follicles were of various sizes, lined with flattened cuboidal cells, distended with colloid, and surrounded by dense hyaline connective tissue trabeculae. Some of the larger follicles showed hyperplasia of the lining epithelium with formation of papillary buds and resorption of colloid. There were a few areas of empty follicles and nests of epithelial cells.

In September, 1939, the patient was enjoying good health. She no longer had symptoms of pressure upon the trachea. She appeared to have a normal thyroid balance. There was no palpable thyroid tissue in the neck.

which was far posterior, was exposed by bisecting the overlying thyroid tissue. The cervical portion of the right lobe was then mobilized by severing the tracheal attachments, the upper pole, and the lateral veins. The intrathoracic portion was then freed by finger dissection. Its delivery was difficult, necessitating compression of the trachea. Resection was then performed leaving a small strip of thyroid tissue posteriorly. A light nitrous oxide oxygen anesthesia was administered during the delivery of the intrathoracic lobe. At times it appeared as if a tracheotomy with an intratracheal catheter might be necessary. Limited exploration to the left of the trachea revealed a small nodular mass which it was deemed advisable not to resect on account of the difficulty of the operation thus far. Plain catgut was used for hemostasis. A cigarette drain and a small rubber catheter were placed to the right of the trachea and the wound closed. Except for mild shock after the operation, the convalescence was smooth.

Pathologic Report.—The specimen consisted of a large mass of lobulated red tissue. Microscopic examination revealed the acini of various sizes and distended with colloid. There was considerable lobulating fibrosis. In some areas there were lymphoid collections and epithelial hyperplasia.

On July 16, 1934, a routine x-ray examination showed a moderate widening of the upper mediastinum with a well-defined area of density extending to the right. In spite of its being on the right, it was interpreted as an intrathoracic nodule arising from the left lobe (Fig. 4).



Fig. 4 (Case 3, W.H.L.)—July 16, 1934, tumor mass to right of trachea twenty days after removal of intrathoracic lobe on same side; this mass apparently arose from the left side.

On Sept. 20, 1934, the patient was enjoying good health and had no cough. In December, 1934, she had an upper respiratory infection with a severe cough. Removal of the remaining intrathoracic mass was advised. In April, 1936, the patient had an illness characterized by a severe cough and fever.

On Feb. 21, 1941, she again came under observation. She was having severe coughing spells, nervousness, and palpitation of the heart. X-ray examination showed that the mass noted in July, 1934, had doubled in size. She still did not consent to having it removed (Fig. 5).

partial calcification. Microscopic examination showed nodular areas of thyroid tissue with large cystic acini lined by flattened epithelium and containing well staining colloid. In areas the stroma was hyaline. There were some areas of closely packed acini with cuboidal lining cells. There was some evidence of old hemorrhage and calcification.

On June 11, 1940, the patient was enjoying good health. There was no palpable thyroid tissue in the neck. She appeared to be in a state of normal thyroid balance.

CASE 3 (Hospital No. 22233).—W. H. L., a white woman, aged 51 years, was admitted to the Roper Hospital on June 7, 1934. She had a long history of bronchitis, hay fever, and asthma. Palpitation of the heart had existed for some years. Lately she had been very nervous and had swelling of the ankles. For the previous two months, she had had coughing spells of such severity that she found it difficult to catch her breath. Often she coughed up long plugs of mucus which she had to extract from her throat with her fingers, following which she felt relieved. Her temperature was elevated at times. There had been a recent loss of weight.



Fig. 3 (Case 3, W.H.L.)—Intrathoracic goiter before operation

Physical examination showed a thin, nervous woman with a pulse of 120, and blood pressure of 135/85. There was a moderate sized nodular enlargement of the thyroid gland on each side of the trachea. X ray examination revealed a well defined widening of increased density on each side of the sternum, of greater degree on the right than on the left. The trachea was considerably narrowed at the level of the superior strait and below (Fig. 3).

The diagnosis was nodular goiter, cervical and intrathoracic, with partial obstruction of the trachea. During the preoperative hospital stay of two weeks, the cough practically subsided and the general condition of the patient improved greatly.

On June 20, 1934, operation was performed under local infiltration of novocain. A collar incision was made through the skin and flaps were reflected. A midline incision was made between the prethyroid muscles to the thyroid gland. The trachea,

thyroid approach was made. The trachea was well exposed and the prethyroid muscles on the right divided transversely. There was a small strip of thyroid tissue to the right of the trachea; it had no connection with the intrathoracic mass. With this exposure the intrathoracic mass could not be located, nor could the finger be passed into the thorax. The sternum was bisected for 6 cm. and a flap formed including a portion of the sternum, the clavicle, and the first two ribs. Upon retraction of this flap the intrathoracic mass was readily recognized. It was fixed with forceps and freed anterolaterally by finger dissection. The inferior border could not be reached, the posterosuperior portion was firmly adherent. Being too large to deliver, the capsule was incised and the contents broken down by finger dissection. Delivery was accomplished, but with difficulty, due to the anteriorly placed subclavian artery. The posterosuperior portion was freed with some difficulty from the apex of the thoracic cavity. A nerve firmly adherent to the mass was recognized and unavoidably severed. It was thought to be the phrenic nerve but later proved to be recurrent laryngeal. Fine chromic catgut was used for hemostasis and closure of the muscle layers, alloy steel wire for the sternum, and clips for the



Fig. 6 (Case 4, K.L.A.).—Large, wholly intrathoracic goiter on right, March 4, 1940.

skin. A large rubber tissue drain was inserted into the space formerly occupied by the goiter and brought out through the neck incision. The operation required two hours. Following the operation the patient was in a moderate degree of shock. Otherwise the convalescence was satisfactory. She left the hospital on the twelfth day after the operation. There was a paralysis of the right vocal cord which has persisted to date (Fig. 7).

Pathologic Report.—The specimen consisted of an oval slender nodular mass 11 by 7 by 4 cm. On section the tissue was irregularly fibrotic and partially calcified. There was a stringlike slender piece of fibrous tissue 9 cm. in length. Microscopic examination showed irregularly distended follicles filled with colloid showing areas of cystic degeneration and fibrosis. A slender strip of fibrous connective tissue and fat contained minute imbedded nerve filaments.

On Oct. 10, 1940, she had the appearance of a normal thyroid balance. The incision was firmly healed. She complained of pain in the right shoulder and upper

COMMENT

In Cases 1 and 2, preliminary removal of the contralateral lobe facilitated the removal of the intrathoracic lobe. In Cases 1 and 3, incision of the capsule resulted in such reduction in size as to make delivery possible. In all three cases, while delivery of the intrathoracic lobe was attended by momentary obstruction of the trachea, in no case was an intratracheal catheter necessary.



Fig. 5 (Case 3, W.H.L.).—Feb. 21, 1941, tumor mass has increased greatly in size.

CASE 4 (Hospital No. 32310).—K. L. A., a white woman, 47 years of age, was admitted to the Roper Hospital, April 16, 1940. In June, 1929, she had had (by W. H. P.), at another hospital, a conservative subtotal thyroidectomy for a large nodular colloid goiter involving both lateral lobes and the isthmus, and extending beneath the clavicles on both sides. The pathologic report is not available. The result of the operation was relief for a number of years from the pressure symptoms of which the patient complained. A mild hyperthyroidism was also relieved.

In July, 1930, she complained of a sore throat and a feeling of fullness in her chest. In October, 1934, she stated that she was in good health. Examination revealed the larynx slightly displaced to the left.

The patient again came under observation in April, 1940. Since an attack of influenza two months previously, she had noticed increased breathing difficulty with frequent paroxysms of coughing. She complained also of dysphagia, epigastric distress, and soreness in the right chest. She had become nervous and had lost seven pounds. She brought with her an x-ray film showing the presence of a large, well-defined dense homogenous mass occupying the right upper thorax. The trachea was displaced to the left. Examination of the neck revealed no palpable thyroid tissue. The vocal cords functioned normally. A diagnosis of intrathoracic goiter was made and operation was advised (Fig. 6).

On April 22, 1940, operation was performed. General anesthesia was instituted at the start, inasmuch as the trachea was easily accessible as a result of the previous thyroidectomy; there was no tracheal obstruction demonstrable at the time of operation, and a superior mediastinotomy was going to be necessary. The usual

On July 17, 1941, the blood calcium was 8.6 mg., phosphorus 2.98 mg. Dihydrotaehysterol, 1 c.c., twice a week, and calcium and cod-liver oil were prescribed.

On Aug. 25, 1941, the blood calcium was 7.8 mg., phosphorus 4.03 mg. She had improved to some extent. The dihydrotaehysterol was increased to 1 c.c. three times a week.

On Sept. 26, 1941, the blood calcium was 8.7 mg., phosphorus 3.52 mg. The symptoms of tetany had practically subsided. The dihydrotaehysterol was increased to 1 c.c., six times a week.

On Nov. 7, 1941, the symptoms of tetany had subsided. Blood calcium was 10.6 mg., phosphorus 4.62 mg. Dihydrotaehysterol, 10 mm. daily, was prescribed, also calcium gluconate, 3 Gm. daily.

COMMENT

This patient had an unusually large completely intrathoracic goiter. It was larger than reported by the pathologist as it was reduced in size so as to permit its delivery. Whether it arose from a nodule overlooked at the previous thyroidectomy or from an aberrant rest cannot be determined. A similar case of Allen's was reported by Means.² A mediastinotomy was necessary for the removal of the tumor. An obstacle to delivery was the anteromedially situated subclaviar artery. An adequate airway was maintained without an intratracheal catheter.

SUMMARY

1. In the removal of an intrathoracic goiter the use of the intratracheal catheter has its disadvantages as well as its advantages; it is generally unnecessary.

2. The operative technique whereby the use of the intratracheal catheter may be avoided is described.

3. Four cases are reported.

REFERENCES

1. Higgins, C. C.: Intrathoracic Goiter, *Arch. Surg.* 15: 895-912, 1927.
2. Means, J. H.: Thyroid and Its Diseases, Philadelphia, 1937, J. B. Lippincott Company.
3. Lahey, Frank H.: Intrathoracic Goiter, *J. A. M. A.* 113: 1098-1104, 1939.
4. Sise, L. F.: Development of Anesthesia for Thyroid Surgery, Frank Howard Lahey Birthday Volume, Springfield, Mass., 1940, Charles C Thomas.

right dorsal spine and numbness and tingling of the right hand. Chvostek's sign was positive. Calcium and cod-liver oil were prescribed.

On June 15, 1941, she was nervous. The above symptoms were more pronounced. X-ray examination of chest, shoulder, and spine was negative (Fig. 8). Diagnosis was parathyroid tetany.



Fig. 7 (Case 4, K.L.A.) —Ten days after the removal of intrathoracic goiter



Fig. 8 (Case 4, K.L.A.) —June 14, 1941, one year after the removal of the intrathoracic goiter.

On July 17, 1941, the blood calcium was 8.6 mg., phosphorus 2.98 mg. Dihydro-tachysterol, 1 c.c., twice a week, and calcium and cod-liver oil were prescribed.

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A NEW THEORY CONCERNING THE ETIOLOGY OF RIEDEL'S STRUMA

JOSEPH L. DE COURCY, M.D., CINCINNATI, OHIO

(From the Department of Surgery, De Courcy Clinic)

ALTHOUGH ligneous or woody thyroiditis was described as a specific entity by Riedel in 1896, the etiology of this syndrome is still obscure. My object in presenting this paper is an attempt to explain a new etiology of Riedel's struma. I feel that this disease is the result of a previous perithyroiditis which causes a partial constriction of the vessels entering the gland.

As a disease of the thyroid, Riedel's struma is a relatively rare occurrence. Both sexes are about equally affected, generally during the fourth decade of life. However, the condition may appear in younger or in much older individuals. This condition has occurred in the De Courcy Clinic in about 2 per cent of all thyroidectomies and its incidence appears to be about the same as that of cancer of the thyroid.

In woody thyroiditis, the thyroid is enlarged, smooth, and with a characteristic stony hardness or, as Riedel has described it, "iron hardness." As a rule, the disease involves first one lobe and then the other. Pathologic changes which occur result in gradual conversion of the gland into fibrous tissue through which scattered atrophic acini may be found. In many cases, fixation of the gland to the surrounding tissues takes place and the adherent tissue makes surgery difficult.

SYMPTOMATOLOGY AND DIAGNOSIS

Toxic symptoms are generally entirely absent in the early stages. The basal metabolic rate may be normal. However, as a result of the connective fibrous infiltration and the gradual enlargement of the gland, which causes compression upon the trachea, esophagus, and larynx as well as on the neighboring nerves and blood vessels, more definite symptoms begin to be manifest. Dyspnea and dysphagia are the first signs. The feeling of pressure is usually followed or accompanied by hoarseness, stridor, or even aphonia, due to involvement of the laryngeal nerves.

From a review of the literature, one would judge that the onset of Riedel's struma is not acute. Lee² describes its onset as "insidious," while Fox and Missal³ state that the average duration of symptoms is about seven months. This, however, is not always true. During the past year I have operated upon two patients with Riedel's struma who entered the hospital acutely ill and remained for surgery. I will describe these cases in more detail later in the paper.

Though admittedly difficult, the diagnosis of woody thyroiditis usually can be made prior to operation by the characteristic consistency of the gland and by a normal or mildly elevated basal metabolic rate. This at once differentiates it from diffuse toxic goiter. Carcinoma of the thyroid should be considered but usually occurs in the presence of an already existing goiter. Although the hardness of the gland suggests carcinoma, the absence of nodules and the indefinite borders of the glandular enlargement help further to differentiate Riedel's disease from cancer.

The disease must also be differentiated from acute suppurative thyroiditis. However, in Riedel's disease a rapid subsidence of the temperature and a tendency to fibrous formation rather than suppuration become evident.

Hashimoto's disease, formerly etiologically associated with Riedel's struma by some authors but now quite generally recognized as a separate syndrome (Hertzler⁴), may likewise readily be differentiated from woody thyroiditis. Chronic lymphoid thyroiditis (Hashimoto) is characterized by diffuse and extensive lymphatic infiltration, while in Riedel's disease the regional lymph nodes remain uninvolved. Though other symptoms are somewhat similar, in Hashimoto's disease the enlargement is bilateral, usually occurs in women over forty, and is less fixed and much less adherent than in fibrous thyroiditis.

THEORIES OF ETIOLOGY

The etiology of Riedel's struma or ligneous thyroiditis is still unknown. However, many theories as to its cause have been advanced. Some have been discarded while others still have their adherents. Specific organisms have not been noted consistently in fibrous thyroiditis. It is generally conceded that syphilis and tuberculosis are probably not the cause of this condition. Actinomyces, streptococci, and other organisms have been practically ruled out as etiologic factors.

Among contemporary authors, there are those who adhere to the view that Riedel's struma is a result of a local inflammatory process in the thyroid. This view was held by Graham,⁵ in 1931. He pointed out that in these cases the general body economy is affected only secondarily by reason of the destruction of the thyroid, interference with deglutition, and injuries to important blood vessels and nerves. Such a process, he noted, has its counterpart in other organs and tissues, which may be expected to respond in a similar manner except for the fact that the thyroid is so situated that complications can occur readily.

Much the same view was expressed more recently by Harry.⁶ When discussing the pathogenesis of Riedel's disease, it was his opinion that the evidence suggests the process to be chronic inflammatory in nature. In keeping with this view, he cited such factors as the early stimulation of the gland function, followed by destruction of the parenchyma, ex-

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being compressed by the exudate. Conversely, large vessels may be held patulous by the induration.

In his review of the subject, Harry⁶ has noted the variation in the condition of the blood vessels in different specimens of Riedel's struma. He observed that pronounced thickening of the arterioles and small arteries is the rule but that in some cases these vessels appear to be normal. He also noted that the number of capillaries is reduced.

Before going further into a discussion of my views on the etiology of woody thyroiditis, I am going to present briefly two recent cases together with the microscopic findings. These case histories, I feel, will help to clarify my theory.

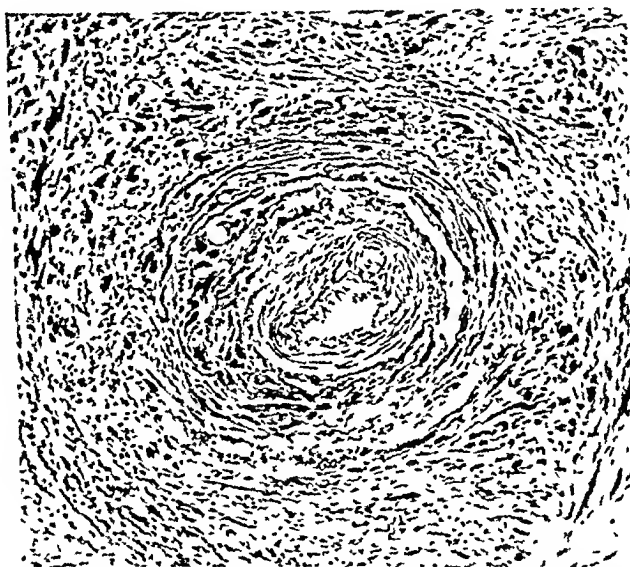


FIG 1—A small artery showing hypertrophy of media with reduction of lumen and surrounding collar of dense hyalinized connective tissue, Hortega silver impregnation stain

CASE REPORTS

CASE 1—V. P., a 42 year old white, married female, entered the Clinic on Nov. 8, 1941, because of loss of weight and nervousness. She presented a history of sore throat, which had occurred one month previously but no history of goiter. Her temperature was 102° F; blood count, 17,800 white cells per c c., differential, polymorphonuclears 73 per cent, small lymphocytes, 25 per cent; eosinophiles, 1 per cent; basophiles 1 per cent. Lung fields and heart were normal. Wassermann and Kahn tests were negative.

Her thyroid was symmetrically enlarged, each lobe being about three times normal size. Her neck overlying the gland was exquisitely tender, with no evidence of external inflammation.

She was referred back to her family physician who kept an icebag on her neck and ordered her to remain in bed. Sulfathiazole, 10 gr., was given every four hours for four days. However, because of the persistence of her symptoms, she was admitted to the Good Samaritan Hospital on Nov. 14, 1941.

tensive fibrosis, the presence of cells usually found in chronic inflammatory states, and the presence of similar lesions in the adjacent cervical tissues.

A somewhat modified concept has been presented by McKnight.⁷ Remarking that we are prone to forget the fact that inflammatory reactions can be brought about by causes other than bacterial invasion, he suggested that the pathologic picture of Riedel's thyroiditis is due to some as yet obscure biochemical irritant differing from that produced in or causing exophthalmic goiter.

More recently, in describing a case of Riedel's struma in a 33-year-old woman, Zelle and his associates⁸ expressed the belief that the disease was caused by abnormal response of the thyroid to physiologic demands.

Conversely, some workers completely doubt the inflammatory nature of the disease. However, there is no convincing evidence to support the view that woody thyroiditis results from adrenal dysfunction or from the degeneration of a previously enlarged thyroid (Harry⁶). Nor is there any satisfactory explanation to be found in embryologic considerations (Zelle and co-workers⁸).

ROLE OF PERITHYROIDITIS

From the foregoing, it would appear that the consensus of opinion up to the present is that Riedel's struma involves the capsule from within and in extreme cases extends far beyond the capsule into the adjacent muscles of the neck. It is my opinion, however, that the true cause is a perithyroiditis and I believe that the fibrous growth begins outside of the gland proper rather than inside the thyroid itself.

That this perithyroiditis always accompanies Riedel's struma in younger persons is demonstrated by the close adherence of the overlying muscles to the gland. It is the purpose of this paper to discuss whether this perithyroiditis is primarily responsible for the woody consistency of the gland or whether it results secondarily from the disease itself.

It has always seemed to me that Riedel's struma is a vascular rather than a glandular disease, one that begins with a perithyroiditis resulting in secondary changes in the gland itself. In this connection, I should like to mention the work of Goldblatt and his associates.^{9, 10, 11} In their extensive experimental studies on hypertension, they clearly demonstrated the profound effect of partial occlusion of the renal blood vessels on specific organs and tissues. The fibrous whorls which we find about the blood vessels in Riedel's thyroiditis are very similar to those described by these investigators.

It is possible that the perithyroiditis with the adherent muscles causes a constriction of the thyroid vessels and their superficial tributaries, thus bringing about the fibrous changes which we find in Riedel's disease. Hertzler,⁴ in discussing the pathology of this disease, states that the cut surface of the hard, fixed mass is bloodless, the smaller vessels

tion. In five days she returned to normal but the thyroid remained enlarged and hard, although the tenderness had disappeared.

Bilateral subtotal thyroidectomy was performed on Nov. 21, 1941.

Examined grossly, the appearance of the excised gland was definitely one of Riedel's struma. The organ was white and muscle fibers in large numbers had densely adhered high over the side of the lobes, which had to be removed by sharp dissection. There was very little bleeding from the cut surfaces. The outer portion of the lobe was most involved and thyroid tissue could be seen beginning about 1 cm. from the capsule. However, the colloid appeared to have a whitish color rather than the red color usually seen.

Dr. William German, pathologist to the Good Samaritan Hospital, reported the following microscopic findings: There was compensatory hyperplasia, intense fibrosis, marked strangulation of functioning thyroid elements, marked arteriosclerosis, formation of pseudogranulomata and pseudogiant cells. The diagnosis was Riedel's struma.

The postoperative period was uneventful. Her temperature reached normal on the fourth postoperative day and remained afebrile at the time of her dismissal.

She has since regained her normal weight and is taking desiccated thyroid, 1 gr. daily, one month after her operation.

CASE 2.—E. K., a 59-year-old, single, white female, entered the Clinic on Sept. 10, 1941. Four weeks prior to admission she had become aware of increasing nervousness, loss of weight, tachycardia, and, at times, a choking sensation in her throat. At the time of admission her temperature was 99° F.; pulse, 88; respiration, 22; blood pressure, 168/90; basal metabolic rate, plus 20. Her thyroid was diffusely enlarged, about two and one-half times normal size, and was quite tender to touch. There was no evidence of external inflammation.

No history of previous goiter could be ascertained, although the patient thought that her neck had appeared to be somewhat swollen over the past four years. However, it had not been as hard as at present. Her blood picture was as follows: hemoglobin, 86 per cent; red blood cells, 4,280,000; white blood cells, 12,800; differential count: polymorphonuclears, 76 per cent, small lymphocytes, 23 per cent, basophiles, 1 per cent. The remainder of the physical examination was essentially negative except for a fine tremor of the hand.

A diagnosis of woody thyroiditis was made and Lugol's solution, 10 drops three times daily, was given.

A subtotal thyroidectomy was performed on Sept. 8, 1941.

The gross pathologic findings in this instance were essentially similar to those found in the previous case; namely, the whitish appearance, the adherent muscles, etc.

The microscopic examination was reported by Dr. William German as follows: There is replacement of thyroid by diffuse struma fibrosa in which there is extensive strangulation of gland-bearing tissue, advanced fibrosis, islands of lymphoid tissue, and formation of pseudogranulomata and pseudogiant cells. There is also marked arteriolar sclerosis. The diagnosis: Riedel's struma.

Forty-eight hours after operation, the patient's temperature became normal and remained so at the time of dismissal on the fifth postoperative day.

DISCUSSION

These cases are interesting because of their acute onset, evidently associated with a perithyroiditis, the tenderness of the overlying structures, and the elevated temperature which subsided quickly with no tendency to suppuration. Of course, one might say that these febrile periods were only exacerbations of an already existing condition. How-

While in the hospital, her temperature range was between 98° and 102° F. Her pulse was 88; respiration 22; blood pressure, 138/78; basal metabolic rate (two readings), plus 16. No medication was given during this time except Lugol's solu-

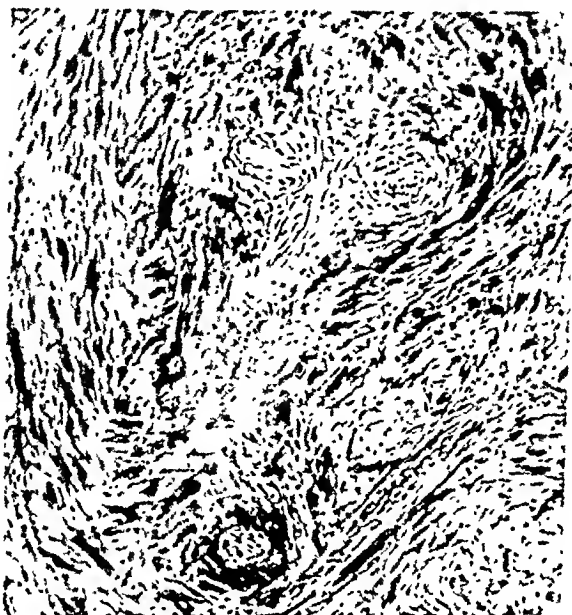


Fig. 2A.

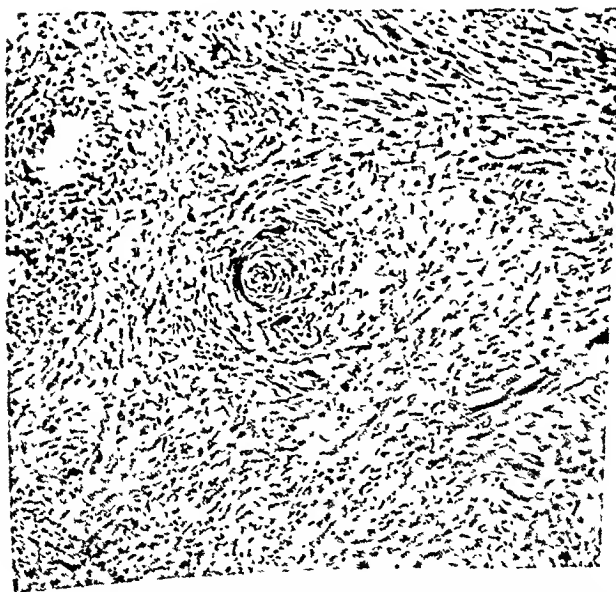


Fig. 2B.

Fig. 2.—A small artery showing medial hypertrophy and a precapillary arteriole showing sclerosis, obliteration, and surrounding collar of dense hyalinized connective tissue; marked hyalinization of the entire stroma. (Hortega silver-gold impregnation stain.)

thyroiditis. Possibly several years would have elapsed before surgery was undertaken and a definite diagnosis made.

It is pertinent that Hertzler,⁴ in discussing Riedel's struma, stated that "whatever the disease may be, it is neither a true inflammation nor a true tumor." Considering the clinical and pathologic findings, it might be said that these cases were instances of acute nonsuppurating thyroiditis which became chronic. If this is true, and I have operated in a sufficient number of cases of Riedel's struma to know the condition when I see it, then it is possible for acute nonsuppurative thyroiditis to metamorphose quickly into chronic nonsuppurative thyroiditis or Riedel's disease.

Considered grossly, these cases cannot be mistaken even if seen early, but it is possible that perithyroiditis has been mistaken for acute nonsuppurative thyroiditis.

We were rather fortunate in obtaining sections from the first case, which we consider to be a very early stage of the disease. In this instance, the surrounding glandular tissue was involved, while recognizable thyroid tissue still remained in the interior of the gland. Thus, it appears that the spread of the fibrous tissue and other pathologic changes occurs from without inward rather than from within outward.

These findings definitely tend to confirm my view that a perithyroiditis is primarily responsible for the woody consistency of the gland and that this fibrous formation does not result from the diseased gland itself. In connection with this last point, I should like to state that I have never seen a true case of Riedel's struma associated with a pre-existing goiter, although such cases have been reported.

Perithyroiditis appears to have been a neglected topic in the medical literature. Not even in standard textbooks have I been able to find any mention of perithyroiditis and yet it is not uncommon to find evidence of it when operating for goiter. Most surgeons know that it frequently becomes necessary to use sharp dissection in freeing nodular goiters from their beds. I cannot account for this except by assuming that a perithyroiditis previously existed. In fact, I feel that I am now encountering more of these cases than in years past.

It is possible that the sudden attempted involution which takes place following the administration of iodine in nodular goiter might account for this apparent fixation, but this will have to be proved. Indeed, Boyden, Collier, and Bugher¹² have suggested that iodine administration may be the causative agent in Riedel's struma. However, Zelle and his associates,⁸ who cite this theory, remark: "It also seems to us that Riedel's struma was observed before Lugol's solution was used for goiter therapy." These workers also note that this hypothesis does not seem to be convincing in the case which they reported, since the patient had not received this drug for any length of time or in any great quantity.

ever, both women were sufficiently intelligent to consult a physician immediately and they would certainly have noticed a hardness in the neck had it existed previously.

It is my opinion that if these patients had not been operated upon, the cases would probably have been classified as acute nonsuppurating



Fig 3A

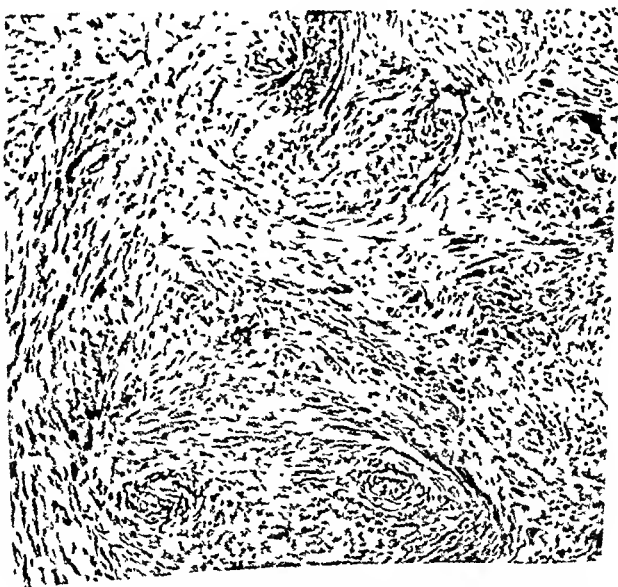


Fig 3B

Fig 3 —Photomicrograph showing sclerosed arterioles and obliteration of thyroid acini by fibrous tissue, Heitega double silver-gold impregnation stain

FRACTURES OF THE NECK OF THE FEMUR

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IT IS very unusual to observe the two distinct types of fracture of the neck of the femur involving both hip joints of the same individual. I have treated two patients with this interesting situation and wish to report the two cases because the radiograms (Figs. 2 and 3) provide excellent material for instruction.

The two types of fracture of the femoral neck are the abduction or impacted fracture, and the adduction or nonimpacted fracture (Fig. 1). The history, clinical examination, radiographic findings, treatment, prognosis, and complications are so different in each of the two types that their proper recognition is essential.

Since the abduction or impacted fracture of the femoral neck requires no special treatment and always unites, it may be that the study

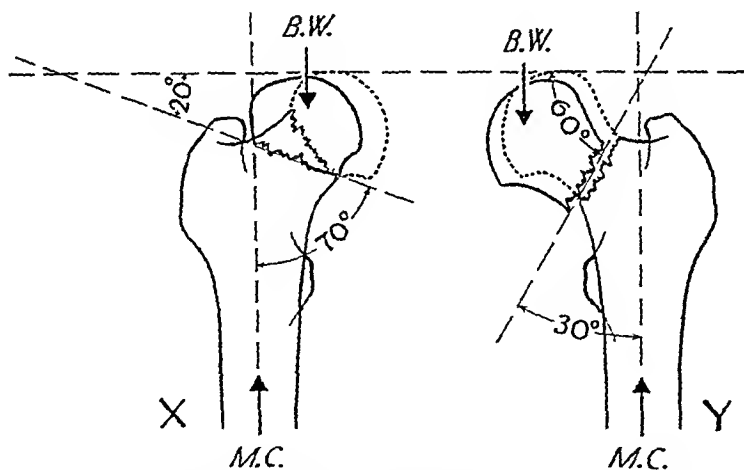


Fig. 1—X, Abduction or impacted fracture; Y, adduction or nonimpacted fracture; B. W., body weight; M. C., muscle contraction. The degree of shearing or pressure forces can be expressed by a study of the angle formed between the fracture line and the horizontal line between the two anteroposterior views (Pauwels) or the angle formed by a line passing a line continuing the axis of the shaft of the femur by Eyre-Brook and Pridie.) The degree of displacement, pressure, and shearing between the fragments should also be studied in the lateral radiograms.

of this type of fracture, Fig. 2 (x) and Fig. 3 (x), will provide information for understanding some of the problems which are encountered in the adduction or nonimpacted fracture, Fig. 2 (y) and Fig. 3 (y). Study of the impacted fracture helps to understand some of the under-

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This last observation likewise holds true in the two cases which I have reported here. In neither instance was treatment with Lugol's solution either prolonged or in large dosage.

We do know, however, that the spectacular involution which follows the use of iodine in diffuse hyperplastic goiters is not forthcoming in the nodular toxic variety. This might possibly be due to the inability of the iodine to reach the glandular tissue because of the dense capsular thickening in these cases, and it is possible that a chemical perithyroiditis (lymphangitis) is effected in the surrounding tissues.

SUMMARY

Let me summarize my views on the etiology of Riedel's struma. It is my opinion that this condition is a vascular rather than a glandular disease, the changes progressing from the outside of the gland rather than from within the organ itself. It begins with a perithyroiditis which induces constriction of the thyroid vessels and associated blood channels. The tissues of the thyroid respond to this ischemia by the formation of the ligneous tissue characteristic of Riedel's thyroiditis.

REFERENCES

1. Riedel, B.: The Chronic Iron Hard Tumor Formation Resulting From Thyroid Gland Inflammation, *Verhandl. d. deutsch. Gesellsch. f. Chir.* 25: 101, 1896.
2. Lee, J. G.: Chronic Nonspecific Thyroiditis, *Arch. Surg.* 31: 982, 1935.
3. Fox, N., and Missal, S.: Riedel's Struma, *Arch. Otolaryng.* 33: 384, 1941.
4. Hertzler, A. E.: Diseases of the Thyroid Gland, New York, 1941, Paul B. Hoeber, Inc., pp. 337, 362, 364.
5. Graham, A.: Riedel's Struma in Contrast to Struma Lymphomatosa (Hashimoto), *West. J. Surg.* 39: 681, 1931.
6. Harry, N. M.: Riedel's Disease and Lymphadenoid Goiter, *M. J. Australia* 2: 395, 1940.
7. McKnight, R. B.: Riedel's Thyroiditis; Suggestion as to Etiology and Surgical Management, *South. Surgeon* 5: 375, 1936.
8. Zelle, O. L., Vass, A., and Steet, A. E.: So called Chronic Thyroiditis With Giant Cells, *Am. J. Surg.* 44: 453, 1930.
9. Goldblatt, H., Lynch, J., Hanzel, R. F., and Summerville, W. W.: Studies on Experimental Hypertension; Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, *J. Exper. Med.* 59: 347, 1934.
10. Goldblatt, H.: Studies on Experimental Hypertension, Production of Malignant Phase of Hypertension, *J. Exper. Med.* 67: 809, 1938.
11. Goldblatt, H.: Experimental Hypertension Induced by Renal Ischemia, *Bull. New York Acad. Med.* 14: 523, 1938.
12. Boyden, A. M., Collier, F. A., and Bugher, J. C.: Riedel's Struma, *Tr. Am. A. Study Goiter*, pp. 35-62, 1935.

lying principles involved in the healing process of fractures of the femoral neck and the importance of mechanical factors on physiologic processes.

The two types of fracture are contrasted in Table I.

The one fundamental principle which is demonstrated by comparing the two types of fracture of the femoral neck is the influence of shearing strain on the healing process of the fracture. In the more common adduction type of fracture, weight-bearing and muscle contraction cause a shearing strain between the fragments with resulting motion, irritation, hyperemie decalcification, absorption of the femoral neck, and nonunion, as shown in Fig. 2 (y). To prevent this unfavorable prognosis, the fresh adduction fracture must be accurately reduced and the reduction must be maintained by efficient internal fixation, as in Fig. 3 (y), with minimum shearing and maximum pressure forces.

In the rarer abduction type of fracture of the femoral neck, the mechanical forces between the two fragments cause, not shearing, but pressure and impaction. These fractures always unite with bony union without any special form of treatment.

The comparison of these two types of fracture of the femoral neck again emphasizes the principles expressed by Roux and Pauwels that pressure forces between fractured bone fragments stimulate bone production. Shearing strains inhibit bone production and cause irritation,

Fig. 2.—X, (1) Injury six years previously; (2) abduction type of fracture of neck of femur; (3) impaction of fragments by pressure forces; (4) coxa vara deformity; (5) almost horizontal subcapital fracture line (30° angle with the horizontal); (6) there was no displacement or shearing of fragments in the lateral radiogram; (7) pressure forces between the fragments dominated over shearing forces; (8) no special treatment except crutches for several weeks after the injury; (9) solid bony union resulted; (10) no aseptic necrosis after six years; and (11) perfect function of the extremity six years after the injury.

Y, (1) Injury ten months previously; (2) adduction type; (3) no impaction of fragments because shearing forces dominated; (4) coxa vara deformity; (5) fracture line is more vertical and forms an angle of more than 50° with the horizontal; (6) there was displacement and shearing of fragments; (7) pressure forces between the fragments dominated over pressure forces; (8) no special treatment except crutches for several weeks after the injury; (9) solid bony union resulted; (10) no aseptic necrosis of the femoral head after ten years; and (11) perfect function of extremity ten years after injury.

Fig. 3.—X, (1) Injury ten years previously; (2) abduction type of fracture of femoral neck; (3) impaction of fragments because of pressure forces; (4) coxa vara deformity; (5) almost horizontal subcapital fracture line which formed an angle of about 30° with the horizontal; (6) no displacement or shearing of fragments in the lateral radiogram; (7) pressure forces between the fragments dominated over the shearing forces; (8) no special treatment except crutches used for several weeks after the injury; (9) solid bony union resulted; (10) no aseptic necrosis of the femoral head after ten years; and (11) perfect function of extremity ten years after injury.

Y, (1) Injury two and one-half years previously; (2) adduction type of fracture of femoral neck (original x-ray studies); (3) no impaction because of shearing (original); (4) coxa vara deformity (original); (5) transcervical fracture line which formed an angle of about 30° with the horizontal (original); (6) displacement and shearing of fragments; (7) pressure forces between the fragments dominated over the pressure forces; (8) the fresh fracture was treated by reduction of the fragments and immobilized with a Smith-Petersen nail, the fragments were immobilized with a Smith-Petersen nail in order to eliminate shearing forces and to contribute to bone production; (9) solid bony union of the fracture, no absorption of the femoral neck and no aseptic necrosis of the femoral head two and one-half years after injury, as demonstrated in the above radiogram; (10) perfect function two one-half years after reduction and nailing of fracture; and (11) present age, 81 years.



FIG. 2. (For legend see opposite page.)



FIG. 3. (For legend see opposite page.)

hyperemie decalcification, absorption of the neck of the femur and non-union. Aseptic necrosis of the femoral head resulting from failure of revascularization is intimately related to the degree of shearing.

The degree of shearing or pressure can be expressed by a study of the angle formed between the fracture line and the horizontal line between the two anterosuperior iliac spines or the angle formed between the fracture line and the shaft-axis line (Fig. 1). This study of mechanical forces should be routine in the examination of all fractures of the neck of the femur because they play a most important role in treatment and prognosis.

REFERENCES

- Watson-Jones, R.: *Fractures and Other Bone and Joint Injuries*, Edition 2, Baltimore, 1941, Williams & Wilkins Company.
- Gaenslen, F. J.: Fracture of the Neck of the Femur (Sir Robert Jones Lecture in Orthopedic Surgery), *J. A. M. A.* 107: 105-114, 1936.
- Hart, Vernon L.: Impacted Fracture of the Hip, *SURGERY* 11: 472-473, 1942.
- Eyre-Brook, A. L., and Pridie, K. H.: Intracapsular Fractures of the Neck of the Femur. Final Results of 75 Consecutive Cases Treated by the Closed Method of Pinning, *Brit. J. Surg.* 29: 115, 1941.

TABLE I
FRACTURES OF THE NECK OF THE FEMUR

TYPE	ABDUCTION OR IMPACTED; ♂ IN RADIOGRAMS	ADDUCTION OR NONIMPACTED; ♀ IN RADIOGRAMS
Incidence	15-20 per cent of all fractures of neck of femur	50-85 per cent
Pain and muscle spasm	Slight	Severe
Disability	May walk after injury without assistance	Marked disability
Deformity of the extremity	No fixed deformity	Adduction and external rotation deformity
Shortening	No	Yes
X-rays	<ol style="list-style-type: none"> 1. Always a subcapital fracture line 2. Always a coxa valga deformity, never a coxa vara deformity 3. Almost horizontal fracture line which forms an angle of not more than 30° with the horizontal line through the anterosuperior iliac spines 4. Impacted fragments because of pressure forces 5. No displacement or shearing of fragments in lateral radiogram 6. Pressure forces between the fragments dominate in both anteroposterior and lateral views 7. Abduction of the distal fragment in relation to the 	<ol style="list-style-type: none"> 1. Subcapital, transcervical, or basal fracture line 2. Coxa vara deformity 3. Fracture line forms an angle of 30 to 90° with the horizontal 4. There is no true impaction. The fragments may overlap slightly and seem to be impacted but are merely entangled. There is a false or pseudo impaction but never a true impaction 5. Frequent displacement and shearing force in the lateral radiogram 6. Shearing forces dominate over pressure forces in both anteroposterior and lateral views 7. Adduction of the distal fragment in relation to the
Treatment	no plaster splint, no internal fixation. Encourage motion and weight bearing	internal fixation to maintain the reduction with minimum shearing and maximum pressure forces
Bony union	Always unite	High percentage if properly reduced and immobilized by internal fixation
Absorption of femoral neck and non union	No	Frequent if not accurately reduced and properly immobilized by internal fixation
Aseptic necrosis	Infrequent	Relatively frequent
End result	Perfect function if not complicated by aseptic necrosis of femoral head	Depends on accuracy of reduction, efficiency of internal fixation, and complications resulting from circulatory damage and shearing strain

anomaly. The slight increase in length which frequently follows the healing of a fracture seldom necessitates operative intervention.

Length of legs may be equalized by shortening the long leg, by lengthening the short leg, by stimulating growth in the short leg, or by retarding growth in the long leg. Epiphyseodiaphyseal fusion, as described by Phemister, is of definite value in the treatment of inequality in length of the legs during the growing period. The operation usually is performed on the epiphysis at the lower end of the femur or on the epiphyses at the upper end of the tibia and fibula, or on both; arrest of longitudinal growth of the bones, thus, is obtained.

Still in the experimental stage are the operations for activating the epiphyses and for stimulating longitudinal growth of bones either by interruption of medullary blood supply¹⁸ or by peripheral vasodilatation following excision of the lumbar sympathetic rami and ganglia.^{23, 29} To date, the results obtained by these procedures are neither spectacular nor convincing. In experimental studies of four normal goats and of one monkey which had residual paralysis from anterior poliomyelitis, Bisgard observed that longitudinal growth of bone was not influenced by sympathetic de-innervation.

We shall limit our discussion in this paper to consideration of the first two methods of leg equalization, that is, leg shortening and leg lengthening.

LEG SHORTENING

The earliest report of a case of operative bone shortening was made by Sayre in 1863; he performed a simple oblique osteotomy of a femur and allowed the fragments to override. Glaessner, in 1907, reported three similar cases. Deutschländer, Calvé and Galland, Taylor, and Groves, suggested procedures for compensatory shortening of the unaffected femur. More recently, White (1935) recommended transverse osteotomy of the femur with overlapping of the fragments and insertion of removable pins to maintain the fragments in correct position. This is a simple and quite satisfactory operative procedure for shortening of the femur. The first report of a case of shortening of the tibia and fibula was made by Brooke,¹¹ in 1927, and his method is still one of the best employed today.

In a survey of the literature, Wilson and Thompson collected reports of 100 cases of bone shortening, contributed by five authors. In this series there were ninety-eight femoral shortenings and two tibial shortenings. The average shortening obtained was 5 cm.; there were seven cases of postoperative infection and two cases of delayed union.

During the period from 1933 to 1940, inclusive, operations for bone shortening were performed in nineteen cases at the Gillette State Hospital for Crippled Children. The essential data in these cases are summarized in Table I. There were twelve operations on the femur

EQUALIZING THE LOWER EXTREMITIES: A CLINICAL CONSIDERATION OF LEG LENGTHENING VERSUS LEG SHORTENING

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LOWER extremities unequal in length often produce deleterious effects on the patient from both a mechanical standpoint and a psychologic standpoint.

Mechanically, no more than 4 cm. of shortening of one leg may be compensated for by a tilting of the pelvis; when the shortening is more than this amount, a lift usually must be inserted into the shoe of the short leg to prevent the development of an excessive curvature of the spinal column. Scoliosis and poor posture, with resultant symptoms of strain and fatigue, commonly result from an uncorrected inequality in length of the legs.

Psychologically, a shortened lower extremity because of its attendant disadvantages may be harmful. An elevated shoe, especially if the sole is raised more than 2.5 cm., is conspicuous whether the wearer is walking or sitting, and the wearer of such a shoe may become unhappily self-conscious because of his physical handicap. The weight of the elevated shoe may also be objectional for a patient who has partial paralysis of the muscles in the shortened limb. In addition, the expense of specially built shoes during a lifetime is frequently an important consideration because it is a burden.

Anterior poliomyelitis is one of the etiologic agents which most frequently produce a shortening of a lower extremity. Other causes of shortening include malunited fractures, epiphyseal arrest caused by either injury or infection, congenital dislocation of the hip, arthritis of the hip or knee (especially tuberculous), congenital anomalies, tumors, and chronic infections of bone. It is with these conditions that the orthopedist has chiefly to deal in cases of inequality in length of the lower extremities. Of the forty-five cases reviewed in this paper, the shortening of the leg was due to anterior poliomyelitis in thirty-four cases, to epiphyseal arrest in three cases, to congenital dislocation of the hip in three cases, to arthritis of the hip in three cases, to malunited fracture of the femur in one case, and to congenital shortening in one case.

Occasionally, a leg may be caused to grow longer than its fellow by the presence of a chronic infection of bone, a tumor, or some congenital

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TABLE I—CONT'D

CASE	DIAGNOSIS	TYPE OF OPERATION	SHORT-ENING OBTAINED (CM.)	COMPLICATIONS	REMAINING IN-EQUALITY IN LENGTH (CM.)
17	Poliomyelitis	Z osteotomy of tibia; intramedullary graft; vitalium screws	5	Soft tissue infection; delayed union, 8 months	Legs equal
18	Poliomyelitis	Z osteotomy of tibia; vitalium screws	4	None	0.5
19	Osteomyelitis; epiphyseal arrest of femur	Transverse osteotomy of femur; vitalium plate; onlay graft	5	Osteomyelitis; removal of onlay grafts 1 month after operation; wound draining 5 months after operation (at time of report)	Final report not obtained

and seven on the tibia and fibula. Shortening obtained by operation ranged from 4 to 8.5 cm., the average for all the cases being a little more than 5 cm.

The average number of days in the hospital for each of the first eighteen patients in this series was 168; the greatest number, 292; and the least, 101. The majority of the patients began walking with guarded weight bearing, three months after operation. Thomas ring caliper braces were worn for another three to six months in most of the cases of femoral shortening; and walking casts were worn for another six to twelve weeks in most of the cases of tibial shortening.

There are definite disadvantages to the operation of bone shortening. It is most important for the surgeon to realize that this operation is performed on a normal extremity in the presence of an extremity that is already abnormal. This jeopardizing of the well leg makes any post-operative complication all the more serious and costly. A patient who has only one normally functioning leg will think twice before consenting to any elective operative procedure on the well member. A lift on the shoe of the short leg, no matter how unsightly, would certainly be preferable to a postoperative disability of the previously normal longer leg.

If a patient is approximately 6 feet (183 cm.) tall, a bone-shortening operation would ordinarily be recommended rather than a bone-lengthening procedure. However, when the height of the patient is only 5½ feet (168 cm.), or less, the surgeon is not so hasty to suggest a further 2 or 3 inches (5 or 7.5 cm.) shortening of stature. Women, of course, can better afford to lose a few inches in height than can men; short stature is never so much of a physical handicap to a woman as it is to a man. Furthermore, a loss in height may become a mental handicap.

TABLE I
CASES OF LEG SHORTENING

CASE	DIAGNOSIS	TYPE OF OPERATION	SHORT-ENING OBTAINED (CM.)	COMPLICATIONS	REMAINING INEQUALITY IN LENGTH (CM.)
1	Poliomyelitis	Z osteotomy of femur; vitallium screws	8.5	None	Legs equal
2	Poliomyelitis	Z osteotomy of tibia; bone screws	5.5	Slight anterior bowing	Legs equal
3	Poliomyelitis	Dovetail tibia; bone screws and Parham band	6.5	Slight posterior bowing; removal Parham band and bone screws	1
4	Congenital dislocation of hip	Z osteotomy of femur; bone screws	8	Separation at osteotomy site; corrected by manipulation	Legs equal
5	Syphilitic epiphysitis	Z osteotomy of femur; Anderson screw	4	None	Legs equal
6	Poliomyelitis	Z osteotomy of femur; Anderson screw	5	Moderate degree relaxation of knee; osteotomy femur to correct lateral bowing 10 months after operation	Legs equal
7	Congenital dislocation of hip	Osteotomy of femur; intramedullary graft	5	None	Legs equal
8	Poliomyelitis	Osteotomy of tibia; intramedullary graft	4.5	Fracture of intramedullary graft 11 months after operation	Legs equal
9	Septic arthritis of hip	Oblique osteotomy of femur; steel nail	5	None	Legs equal
10	Congenital dislocation of hip	Osteotomy of femur; Anderson screw	4.5	Superficial infection; slight anterior bowing	3
11	Tuberculosis of hip	Dovetail femur; nail and wire	4	Slight anterior bowing	5
12	Poliomyelitis	Osteotomy of tibia; intramedullary graft	4	None	Legs equal
13	Poliomyelitis	Z osteotomy of femur; chrome catgut	7.5	Fracture through callus; slight anterior bowing	Legs equal
14	Poliomyelitis	Z osteotomy of tibia; ivory screws	5	Delayed union, 12 months	Legs equal
15	Poliomyelitis	Z osteotomy of femur; Parham bands	3	Osteomyelitis; removal of bands and sequestrum; healed 27 months after operation	3
16	Poliomyelitis	Z osteotomy of femur; wire and two bone screws	4	None	Legs equal

tions included infection in twenty-two cases, delayed union in five cases, nonunion in twelve cases, fracture in ten cases, and injuries to nerves in five; there was one death.

During the period from 1928 to 1940, inclusive, operations for leg lengthening were performed in twenty-six cases at the Gillette State Hospital. Table II presents a summary of data in these cases. There were two cases of femoral lengthening, twenty-three cases of tibial lengthening, and one case in which both femur and tibia were lengthened. The amount of lengthening obtained by operation ranged from 0.5 to 7.5 cm., the average for all cases being 4.5 cm.

The average number of days in the hospital for each of the patients in this series was 244.5, the greatest number was 552, and the least number, 87. The patient who stayed in the hospital 552 days had a lengthening of both tibia and femur. The majority of the patients began walking, with guarded weight bearing, about four months after operation. Thomas ring caliper braces or short Hessing braces were worn for another three to six months in most of the cases.

From the data recorded in Table II it is evident that no one of the three femoral-lengthening operations was satisfactory. In each of the three cases an attempt was made to obtain lengthening without skeletal countertraction. We agree with Putti³² and Abbott² that skeletal countertraction is an essential principle of a leg-lengthening procedure.

In most of the cases, of which Figs. 1, 2, and 3 are typically illustrative, a tongue and groove osteotomy of the tibia was performed. The steps of this operation are as follows: tenotomy of the Achilles tendon, transverse osteotomy of the fibula, insertion of one Steinmann pin in the lower end and two pins in the upper end of the tibia, tongue and groove osteotomy of the tibia between the pins, cutting of all tight fascial and periosteal bands, and application of the leg-lengthening apparatus. The osteotomy of the tibia is performed through a long, curved, anteromedian incision; the tibial shaft is exposed, and, with the double blade motor saw, a long double cut is made through the anterior osseous cortex. These two vertical saw cuts are joined below by a transverse cut anteriorly and above by means of Gigli's wire saw posteriorly. This leaves the tongue graft above and the groove below.

The apparatus employed in all of the tibial lengthenings was a modification devised by Cole, in 1927, of Abbott's original apparatus. This modified apparatus enables the surgeon to carry out the three principles so necessary for a successful operation for leg lengthening, that is, employment of skeletal traction and countertraction, application of slow continuous traction, and maintenance of accurate contact and alignment of the fragments.

Before an operation for leg lengthening is performed, the patient should try wearing an elevated shoe, not only to correct secondary conditions such as scoliosis and poor posture, but also to determine the amount of lengthening which will give the optimal improvement in

The shortening may be "humiliating" in the true etymologic sense of the word, "to make nearer the ground."³⁷ A man who is less than 5 feet 5 inches (165 cm.) tall probably would prefer to wear a lift on his shoe for the rest of his life than to lose 2 or 3 inches (5 or 7.5 cm.) in height.

We believe that a leg-shortening operation should not be performed until after the growth of the patient has been well attained. The postponement obviates the necessity of using any formula, such as that recommended by Brooke,³² to determine the additional amount of shortening which will be required after the patient's growth has ceased. In the series of nineteen cases reported herein, the average age of the patients was eighteen and one-half years; the youngest patient was sixteen and the oldest, twenty-one years of age. If, at the time of operation, the cause of the shortening is still active, continuation of the disturbed rate of growth will lead later to discrepancy in the length of the limbs. Some authors suggest that the hyperemia resulting from the shortening operation also may lead to an increased rate of growth of the shortened leg.

LEG LENGTHENING

Surgical procedure for bone lengthening is much newer than that for bone shortening. Codivilla, in 1905, was the first to devise a method for lengthening long bones; he performed osteotomy and then applied direct skeletal traction by means of a nail through the os calcis. In a series of twenty-two cases, Codivilla obtained gains in length of 3 to 8 cm. In 1908, Magnuson demonstrated experimentally that leg lengthening could be performed without damage to the blood supply or nerve function of the extremity. Using an apparatus called an "osteoton," which provided continuous skeletal traction, Pntti,³¹ in 1921, succeeded in obtaining 7.5 to 10 cm. lengthening in ten cases of femoral shortening; in all these cases union was somewhat delayed. It remained for Abbott¹⁻⁴ to devise a simple dependable apparatus, to standardize the operative procedure, and to place the operation of leg lengthening on a practical basis. Since Abbott's first report, in 1927, of six cases in which bones were lengthened successfully, the operation has been performed on hundreds of patients by various orthopedic surgeons throughout the country. There have been, of course, minor variations in the technique of operation and in the lengthening apparatus employed.^{6, 7, 9, 21, 22, 24, 26, 38} Most surgeons prefer to lengthen the tibia and fibula, but Anderson expressed the belief that it is wiser to lengthen the femur.

Wilson and Thompson collected reports of 270 cases of bone lengthening which had been contributed by eleven different authors; of these cases the surgical procedure in 224 was lengthening of the tibia and fibula and in forty-six, of the femur. The maximal amount of lengthening obtained from either the tibia or the femur was 9 cm. and the maximal lengthening from both bones, 11.5 cm. Postoperative complica-

TABLE II—CONT'D

CASE	DIAGNOSIS	TYPE OF OPERATION	LENGTH OBTAINED (CM.)	COMPLICATIONS	REMAINING INEQUALITY IN LENGTH (CM.)
33	Poliomyelitis	Tongue-groove osteotomy of tibia	7	Relieve graft to ulcer of lower leg 5 years after operation; pinch graft to another ulcer 7 years after operation	Legs equal
34	Poliomyelitis	Tongue-groove osteotomy of tibia	6	None	Legs equal
35	Poliomyelitis	Z osteotomy of tibia	2.5	None	2.5
36	Poliomyelitis	Tongue-groove osteotomy of tibia	4	Delayed union, 11 months after operation; supracondylar osteotomy of femur for genu valgum 6 years after operation	5
37	Poliomyelitis	Tongue-groove osteotomy of femur; Roger Anderson apparatus	1	Apparatus removed; 13-pound traction applied; fracture tongue graft	5
38	Congenital shortening	Tongue-groove osteotomy of tibia	4	Drainage upper end of wound; chicken pox	4
39	Poliomyelitis	Tongue-groove osteotomy of tibia	6.5	Removal of protruding portion of tongue graft 5 months after operation; osteomyelitis healed 14 months after operation	1
40	Poliomyelitis	Tongue-groove osteotomy of tibia	7	Lower pin broken and replaced	Legs equal
41	Poliomyelitis	Tongue-groove osteotomy of tibia	4.5	Slight drainage, lower pin	0.5
42	Poliomyelitis	Tongue-groove osteotomy of tibia	4	Lower pin broken and replaced	Legs equal
43	Poliomyelitis	Tongue-groove osteotomy of tibia	7.5	None	4.5
44	Septic arthritis of hip with dislocation	Tongue-groove osteotomy of tibia	5	Temporary peroneal hypesthesia	5
45	Old fracture of shaft of femur	Tongue-groove osteotomy of tibia	5	Tongue graft exposed in incision; fastened with two vitallium screws 7 months after operation; not healed 11 months after operation	1.5

*In Case 31 two operations were performed.

TABLE II
CASES OF LEG LENGTHENING

CASE	DIAGNOSIS	TYPE OF OPERATION	LENGTH OBTAINED (CM.)	COMPLICATIONS	REMAINING INEQUALITY IN LENGTH (CM.)
20	Poliomyelitis	Tongue-groove osteotomy of tibia	3	Lower pin broken before lengthening complete	4
21	Poliomyelitis	Tongue-groove osteotomy of tibia	2.5	Upper pins broken before lengthening complete	4
22	Epiphyseal arrest, septic arthritis of knee	Z osteotomy of femur; tongs in condyles	3	Method of traction not satisfactory	10
23	Poliomyelitis	Tongue-groove osteotomy of tibia	0.5	Lower pin broken; fracture tongue graft; drainage; sequestrectomy 12 months after operation	6.5
24	Poliomyelitis	Tongue-groove osteotomy of tibia	3	Drainage around pins; curettement of sinuses 7 months after operation	6
25	Poliomyelitis	Tongue-groove osteotomy of tibia	2.5	Area around incision slow to heal; persistent ulcer here was grafted 31 months after operation	2.5
26	Poliomyelitis	Tongue-groove osteotomy of tibia	4.5	None	1
27	Poliomyelitis	Tongue-groove osteotomy of tibia	4.5	None	Legs equal
28	Poliomyelitis	Tongue-groove osteotomy of tibia	6.5	Plastic closure sinus 7½ months after operation; curettage of sinus 9 months after operation	Legs equal
29	Poliomyelitis	Tongue-groove osteotomy of tibia	5	Drilling for nonunion 12 months after operation	5
30	Poliomyelitis	Tongue-groove osteotomy of tibia	4	Draining sinuses 6 months after operation	Legs equal
31*	Poliomyelitis	Tongue-groove osteotomy of tibia	5.5	None	5
		Vertical osteotomy of femur	1.5	Upper pin broken; apparatus removed and 20-pound traction to lower pin; drainage about pins; tibial graft for nonunion femur 9 months after operation; fractured shaft femur 39 months after operation	4
32	Poliomyelitis	Tongue-groove osteotomy of tibia	6.5	Fracture tongue graft 5 months after operation	1



FIG. 2.—Lengthening of the tibia and fibula. Case 28: a, anterior view of the patient on admission, right leg 65 cm. shorter than left; b, right tibia and fibula in the leg-lengthening apparatus, five weeks after operation; c, anteroposterior and lateral views of right tibia and fibula, seven months after operation plastic closure of sinus, through which distal end of tongue graft projected, was done at this time; d, anterior view of the patient on discharge, one year after operation; patient is wearing a Thomas' ring caliper brace and legs are equal in length; e, anteroposterior and lateral views of right tibia and fibula, twenty months after operation.

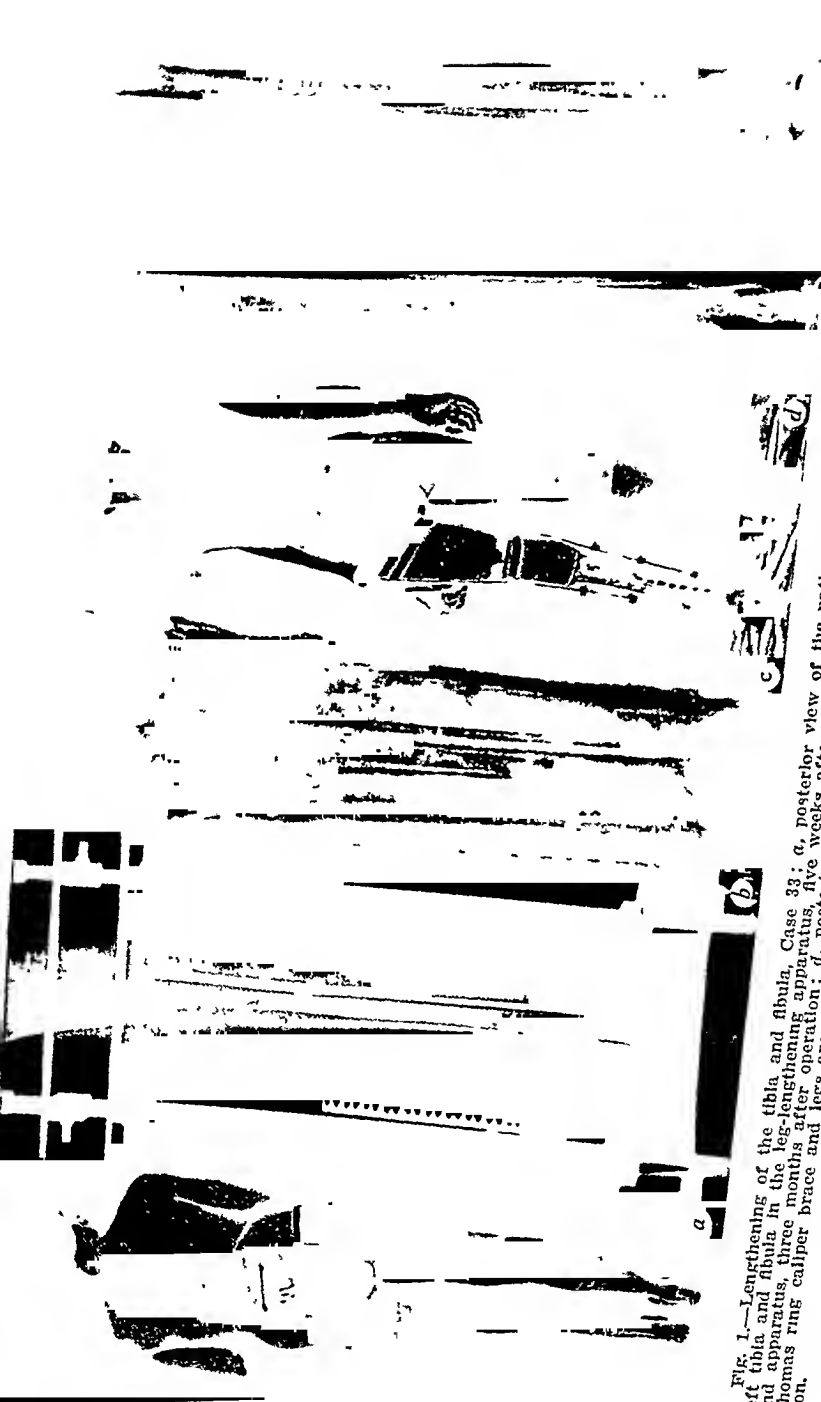


Fig. 1.—Lengthening of the tibia and fibula, Case 23; a, posterior view of the patient on admission, left leg 7 cm. shorter than right; b, left tibia and fibula in the leg-lengthening apparatus, three months after operation; c, left tibia and fibula in plaster cast after removal of brace; d, Thomas ring caliper brace and legs are equal in length; e, anteroposterior and lateral views of left tibia and fibula four years after operation.

function. Whether or not there is a fixed pelvic obliquity should also be determined before operation. If the abductor muscles of the hip are weak, as they frequently are in cases of poliomyelitis, equalization of the lower legs and consequent leveling of the pelvis will so change the leverage of these weakened muscles that the gait may be worse after the lengthening than before the operation. At least one case has been reported in which the hip gradually dislocated after a lengthening operation upon the tibia.²⁷ A child who has very weak hip muscles walks better if the paralyzed leg is at least one-half inch shorter than the normal leg. We believe it is not advisable to perform a leg-lengthening operation of any type unless the quadriceps and abductor muscles of the hip are strong.

An operation for leg lengthening is not indicated unless there is a shortening of more than 2.5 cm. that is producing impairment of gait. Clinical or roentgenographic evidence of previous infection or other pathologic involvement of the bones of the short extremity contraindicates the operation for bone lengthening. Another contraindication is a shortening of so marked a degree that the maximal lengthening even of both the tibia and femur will not sufficiently equalize the extremities. In these rare cases, amputation and the use of artificial limbs will give better functional results.

We believe it is preferable for the patient to be at least 14 to 16 years of age before undergoing the operation, although in this series of twenty-six cases, eight patients were less than 14 years old. The youngest patient was 9 and the oldest 21 years old; the average age for the twenty-six patients was 15½ years of age.

Leg lengthening is a somewhat formidable and technically difficult operative procedure entailing a prolonged period of disability and a risk of numerous complications of which the more important are post-operative infection, delayed union or nonunion, paralysis of nerves caused by stretching, circulatory disturbances (prolonged edema, chronic ulcers, thrombosis, and so forth), breaking of the metal traction pins, and fracture of the tongue graft. Other complications reported in the medical literature^{10, 16, 33, 34} include late fractures, malunion, necrosis of skin and bone, traumatic arthritis and lessened motion in the knee, deformity of the foot, protrusion of the tongue graft through the skin, displacement of the head or the distal end of the fibula when this bone unites prematurely and is not lengthened as much as the tibia, and increased weakness of the lengthened muscles in cases of poliomyelitis. Not all these types of complications occurred in the series of cases reported in this paper; those which were encountered are listed in Table II.

LEG LENGTHENING VERSUS LEG SHORTENING

The operation for lengthening of a shortened extremity always has held an irresistible appeal for surgeons and patients alike. We believe,



Fig. 3—Lengthening of the tibia and fibula, Case 43. *a*, posterior view of the patient, right leg 15 cm. shorter than left; *b*, right tibia and fibula in the leg-lengthening apparatus one month after operation; *c*, right tibia and fibula in plaster cast after removal of pins and apparatus five months after operation; *d*, posterior view of the patient seventeen months after operation; right leg is still 1.5 cm. shorter than left and patient must wear a long leg caliper brace; *e*, anteroposterior and lateral views of right tibia and fibula, twenty-one months after operation. Both bones are very thin.

8. Bissgard, J. D.: Longitudinal Bone Growth; the Influence of Sympathetic Denervation, *Ann. Surg.* 97: 374, 1933.
9. Bosworth, D. M.: Skeletal Distraction of the Tibia, *Surg., Gynec. & Obst.* 66: 912, 1938.
10. Brockway, A.: Clinical Résumé of Forty-six Leg-lengthening Operations, *J. Bone & Joint Surg.* 17: 969, 1935.
11. Brooke, J. A.: Shortening of Bones of the Leg to Correct Inequality of Length, *Surg., Gynec. & Obst.* 44: 703, 1927.
12. Brooke, R.: Bone Shortening for Inequality of Length in Lower Limbs, *Proc. Roy. Soc. Med.* 30: 441, 1937.
13. Calvé, Jacques, and Galland, Marcel: A New Procedure for Compensatory Shortening of the Unaffected Femur in Cases of Considerable Asymmetry of the Lower Limbs (Fractures of the Femur, Coxalgia, etc.), *Am. J. Orthop. Surg.* 16: 211, 1918.
14. Codivilla, A.: On the Means of Lengthening, in the Lower Limbs, the Muscles and Tissues Which Are Shortened Through Deformity, *Am. J. Orthop. Surg.* 2: 353, 1905.
15. Cole, W. H.: Leg Lengthening for Shortening Due to Infantile Paralysis, *Minnesota Med.* 13: 904, 1930.
16. Compere, E. L.: Indications For and Against the Leg-lengthening Operation; Use of the Tibial Bone Graft as a Factor in Preventing Delayed Union, Nonunion, or Late Fracture, *J. Bone & Joint Surg.* 18: 692, 1936.
17. Deutschländer, C.: Die Heinesche Operation der Kontinuitätsverkürzung zwecks Ausgleichung von Längendifferenzen der unteren Gliedmassen, *Ztschr. f. orthop. Chir.* 19: 47, 1907.
18. Ferguson, A. B.: Surgical Stimulation of Bone Growth by New Procedure; Preliminary Report, *J. A. M. A.* 100: 26, 1933.
19. Glaessner, P.: Die Kontinuitätsresektion der langen Röhrenknochen zur Ausgleichung von Verkürzungen, *Ztschr. f. orthop. Chir.* 19: 39, 1907.
20. Groves, E. W. H.: An Address on Stature and Pose; the Problem of Unequal Legs, *Brit. M. J.* 2: 1, 1931.
21. Haboush, E. J.: Principles Governing Treatment of Fractures and Bone Lengthening by Direct Skeletal Means and New Apparatus; Preliminary Report, *SURGERY* 7: 356, 1940.
22. Haboush, E. J., and Finkelstein, Harry: Leg Lengthening With New Stabilizing Apparatus, *J. Bone & Joint Surg.* 14: 807, 1932.
23. Harris, R. L., and McDonald, J. L.: The Effect of Lumbar Sympathectomy Upon the Growth of Legs Paralyzed by Anterior Poliomyelitis, *J. Bone & Joint Surg.* 18: 35, 1936.
24. Janes, E. C.: Experiences in Leg Lengthening, *J. A. M. A.* 105: 1419, 1935.
25. Magnuson, P. B.: Lengthening Shortened Bones of the Leg by Operation; Ivory Screws With Removable Heads as a Means of Holding the Two Bone Fragments, *Univ. Pennsylvania M. Bull.* 21: 103, 1908.
26. Moore, B. H.: A Bone Lengthening Apparatus, *J. Bone & Joint Surg.* 13: 170, 1931.
27. Moore, B. H.: Discussion, *Surg., Gynec. & Obst.* 58: 321, 1934.
28. Moore, J. R.: Tibial Lengthening and Femoral Shortening, *Pennsylvania M. J.* 36: 751, 1933.
29. Peabody, C. W., and Graham, N.: Inequality of Limb Length in Residual Paralysis From Anterior Poliomyelitis, *Physiotherapy Rev.* 17: 56, 1937.
30. Phemister, D. B.: Operative Arrestment of Longitudinal Growth of Bones in Treatment of Deformities, *J. Bone & Joint Surg.* 15: 1, 1933.
31. Putti, Vittorio: The Operative Lengthening of the Femur, *J. A. M. A.* 77: 934, 1921.
32. Putti, Vittorio: Operative Lengthening of the Femur, *Surg., Gynec. & Obst.* 58: 318, 1934.
33. Sayre: Quoted by Steindler, Arthur: *Orthopedic Operations; Indications, Technique and End Results*, Springfield, Ill., 1940, Charles C. Thomas, p. 237.
34. Sofield, H. A.: Clin. North America 19: 69, 1939.
35. Taylor, R. T.: s and Lengthening Short Legs: A New Surgical Proc. Surg. 14: 598, 1916.
36. Teal, Fritz: Operative Lengthening of the Lower Extremities, *Nebraska M. J.* 22: 219, 1937.
37. White, J. W.: Femoral Shortening for Equalization of Leg Length, *J. Bone & Joint Surg.* 17: 597, 1935.
38. Wilson, P. D., and Thompson, T. C.: A Clinical Consideration of the Methods of Equalizing Leg Length, *Ann. Surg.* 110: 992, 1939.

however, that for the majority of patients who have shortening of one of the lower extremities, an operation for leg shortening is preferable to an operation for leg lengthening.

The operation for leg lengthening does have certain decided advantages over the procedure for leg shortening. The latter is performed on the abnormal extremity and the well leg is not jeopardized. Furthermore, height is not sacrificed by an operation for leg lengthening; as we have stated previously, a loss in height may be a marked physical or mental handicap to a patient of less than average stature.

The operation for leg shortening, however, is relatively simple and safe, and the procedure is accurate. The shorter period of disability after an operation for leg shortening as compared with the period of disability after an operation for lengthening means a great saving of time and money for the patient. The short leg nearly always is found to be ill adapted to plastic operations; especially as a result of poliomyelitis, the short leg has weak, atrophic muscles, slender bones (Fig. 3), and a relatively poor blood supply. The sound limb is much better suited than the weakened limb to withstand a major surgical procedure. In most cases of inequality of the lower extremities, the operation for leg shortening offers a mechanical advantage in that lowering of the center of gravity of the body tends to increase bodily stability and improve locomotion.

SUMMARY

There have been presented forty-five cases in which operations for equalization of the lower extremities were performed. Twenty-six of the patients had operations for leg lengthening and nineteen had operations for leg shortening. Although serious complications may be encountered subsequent to either type of operation, the advantages of the procedure for leg shortening greatly outweigh those of the operation for leg lengthening. The latter, more formidable operative procedure had probably best be limited to that small, carefully chosen group of patients who have unequal lower extremities and who are either unwilling or ill able to sacrifice any fraction of their height.

REFERENCES

1. Abbott, L. C.: The Operative Lengthening of the Tibia and Fibula, *J. Bone & Joint Surg.* 9: 128, 1927.
2. Abbott, L. C.: Lengthening of the Lower Extremities, *California & West. Med.* 36: 6, 1932.
3. Abbott, L. C., and Crego, C. H.: Operative Lengthening of the Femur, *South. M. J.* 21: 823, 1928.
4. Abbott, L. C., and S. G. J. R. de C. M.: The Operative Lengthening of the Tibia and Fibula: Report on the Further Development of the Principles and Technique, *Ann. Surg.* 110: 961, 1930.
5. Anderson, Roger: Femoral Bone Lengthening, *Am. J. Surg.* 31: 479, 1936.
6. Anopol, George: Leg Lengthening, *Am. J. Surg.* 43: 422, 1939.
7. Barr, J. S., and Ober, F. R.: Leg Lengthening in Adults, *J. Bone & Joint Surg.* 21: 1033, 1939.

The method of excision and closure which I have used for many years fulfills these two requirements: it maps out the area accurately on the overlying skin; it restores the natural groove between the nates, and so entirely obliterates all space between the skin and the sacrococcygeal fascia.

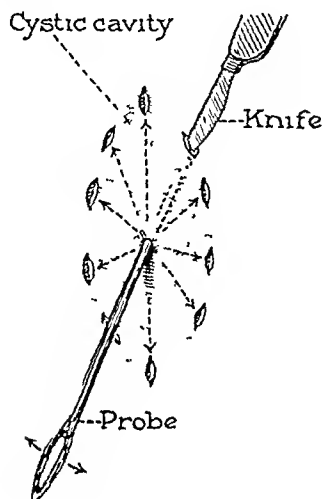


Fig 1

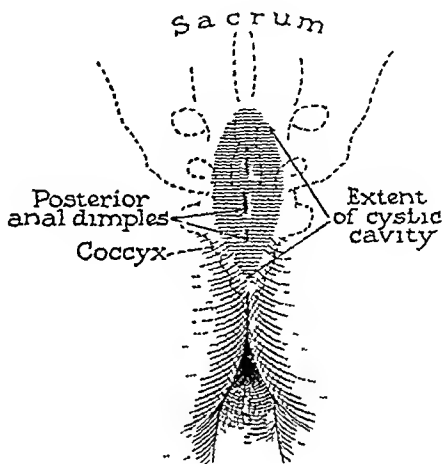


Fig. 2



Fig 3

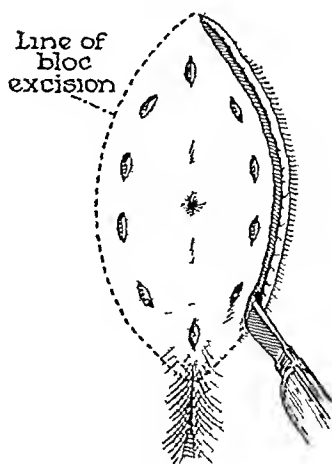


Fig 4

TECHNIQUE

First pass a small probe (Fig. 1) through the postanal dimple (Fig. 2) into the cavity of the cyst and push it cephalad as far as possible

THE SURGICAL TREATMENT OF PILONIDAL CYSTS

WITH A DESCRIPTION OF THE AUTHOR'S METHOD OF DEMARCATION
AND CLOSURE

GUY S. VAN ALSTYNE, M.D., CHICAGO, ILL.

SURGICAL removal of a pilonidal cyst can be facilitated by accurate mapping of the cystic area on the overlying skin. Successful primary closure of the wound is possible only if dead spaces in which blood or serum may accumulate can be prevented.

An almost universal method of mapping out the cyst cavity has been the injection of a methylene blue solution through the sinus that is always present. Gage¹ and others have emphasized that if a dye is injected into these sinuses for the purpose of delineating all of the ramifications of the cyst cavity, it must be injected several days prior to operation. By so doing, the lining will become deeply stained, but the dye will not run and stain newly ent tissue, as happens when its injection is done at the time of operation. The dye method, even with this suggested improvement, however, does not map out the area on the overlying skin, but simply tells the surgeon when he has not excised widely enough.

Many methods of primary closure have been advocated. All have been designed to close accurately the dead space between skin and sacrococcygeal fascia. Lahey,² in 1929, after block excision of the cyst, filled the gap with a pedicle flap. In 1932,³ he modified this by shifting a flap attached at both ends, leaving a crescentic space over one gluteal region to granulate. Cattell⁴ still further modified this in 1934, closing this gap by converting the crescent into a "Y." Burgess⁵ advocates primary closure by undermining the edges of the wound, then placing silk retention sutures tied over a rubber sponge or gauze. This method, he feels, aids in obliterating the dead space in question. Ferguson and Mereray⁶ describe a method of primary suture in which a single mattress suture of alloy steel wire is tied over a gauze roll on either side, or a double mattress suture simulating a double figure-of-eight suture is similarly tied.

In my opinion all of these and similar methods fail to obliterate the dead space between skin and deep fascia because they do not take into consideration the natural depression between the nates in which these cysts usually lie. Instead of restoring this groove, they bridge the skin over it, creating a dead space and so inviting infection.

Read before the Chicago Surgical Society at Wesley Memorial Hospital, Dec. 12, 1941.

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To close,* instead of suturing the edges of the skin flaps to each other, I place mattress sutures of heavy silk very close to the edge of one side, then through the deep fascia overlying the lower sacrum and coccyx in the midline or very slightly past it, then back again through the edge of the same flap (Fig. 5). Sufficient similar sutures are placed along each flap edge from skin to fascia and back so that when tied, each flap is folded on itself with its free edge now held firmly to the bottom of the groove in the midline (Fig. 6). This procedure approximates the edges just as truly as though they were sutured to each other with the additional advantage of entirely obliterating any possible dead space underneath. One or more shallow sutures may be placed from one flap to the other (Fig. 6 A, top suture) should there be any gap, excepting that it is wise, since these cysts are always infected, and since this region is close to the anus, to leave a small gap at the lower angle for drainage.

*The author, in describing this method of closure, had, until April 20, 1942, believed it original with himself. On that date he was informed that practically an identical procedure had been described by Colp[†] in 1929.

REFERENCES

1. Gage, M.: Pilonidal Sinus, *Internat. Clin.* 3: 19, 1936.
2. Lahey, F. H.: An Operation for Pilonidal Sinus, *Surg., Gynec. & Obst.* 46: 109, 1929.
3. Lahey, F. H.: A Further Suggestion for the Operative Treatment of Pilonidal Sinuses, *Surg., Gynec. & Obst.* 54: 521, 1932.
4. Cattell, R. B.: Technic of Operation for Pilonidal Sinus, *S. Clin. North America* 14: 1289, 1934.
5. Burgess, C. M.: Pilonidal Sinus, *West. J. Surg.* 48: 581, 1940.
6. Ferguson, L. K., and Mercray, P. M., Jr.: Pilonidal Cysts; Excision and Primary Suture in Ambulatory Patients, *Am. J. Surg.* 36: 270, 1937.
7. Colp, R.: Treatment of Pilonidal Cysts and Fistulae, *S. Clin. North America* 9: 695, 1929.

using care, however, not to make a false passage into the perieystic tissues. Now make a small nick in the skin over the palpable head of the probe. Next change the position of the probe to an oblique, both right and left, nicking the skin each time over the head as before. Continue this to a transverse position, then obliquely downward and lastly, directly caudad. This series of skin nicks now accurately maps out the cyst area on the skin surface.

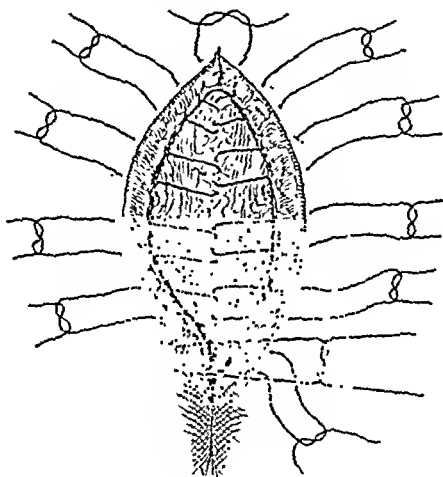


FIG. 5.

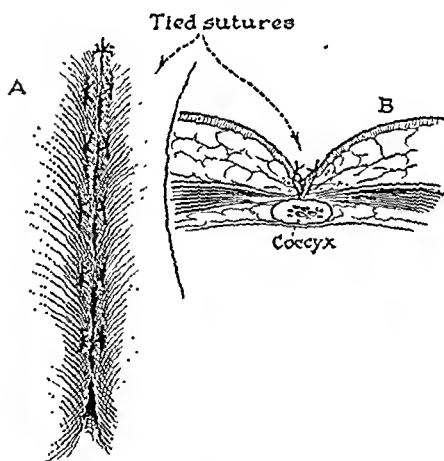


Fig. 6.

Next inject a bismuth paste (Fig. 3). This will distend the cyst, and identify any ramification which an unwary surgeon might inadvertently cut, better, I believe, than methylene blue or other dye can.

With the area accurately delineated on the skin one can now excise the cyst *en bloc* by cutting widely around the marked-out area (Fig. 4).

The following technique was employed for most of the experiments. Eighteen-hour broth cultures of *Staphylococcus aureus* and of *Escherichia coli* were used as test organisms. Various dilutions of the disinfectants were made in 5 c.c. volumes in distilled water. One-half cubic centimeter of a test culture was pipetted into 5 c.c. of each disinfectant, mixed and allowed to stand at room temperature. After five and ten minutes, subcultures were made with an approximately standard phenol coefficient loop into tubes containing about 10 c.c. of (a) plain broth and (b) sodium thioglycolate broth. These subcultures were incubated at 37° C. for a minimum of forty-eight hours and observed for growth. Random subcultures showing growth were stained by Gram's method and examined for contamination but no contamination was observed. Tables I and II are illustrative of the results obtained and represent experiments that were performed at the same time on the germicidal activities of aqueous iodine and mercuric chloride against *E. coli*.

TABLE I
ACTION OF AQUEOUS IODINE PLUS POTASSIUM IODIDE ON *E. coli*

DILUTIONS OF 1% AQUEOUS IODINE PLUS 2% POTASSIUM IODIDE	5-MINUTE SUBCULTURES		10-MINUTE SUBCULTURES	
	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH
Full strength	-	-	-	-
$\frac{1}{4}$	-	-	-	-
$\frac{1}{16}$	-	-	-	-
$\frac{1}{64}$	-	-	-	-
$\frac{1}{256}$	+	+	+	+

+ = Growth
- = No growth } of *E. coli* in ninety-six hours

TABLE II
ACTION OF MERCURIC CHLORIDE ON *E. coli*

DILUTIONS OF $\frac{1}{1000}$ MERCURIC CHLORIDE	5-MINUTE SUBCULTURES		10-MINUTE SUBCULTURES	
	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH
Full strength	-	+	-	+
$\frac{1}{4}$	-	+	-	+
$\frac{1}{16}$	-	+	-	+
$\frac{1}{64}$	-	+	-	+
$\frac{1}{256}$	+	+	+	+

+ = Growth
- = No growth } of *E. coli* in ninety-six hours

Table I indicates that 1 per cent aqueous iodine in dilutions up through $\frac{1}{64}$ apparently killed the test organisms. No growth was observed in the subcultures made into plain broth or sodium thioglycolate broth until dilutions of aqueous iodine exceeding $\frac{1}{64}$ were tested. Table II shows a very contrasting picture. Subcultures into plain broth failed to grow until they were made from an original $\frac{1}{256}$ dilution of the $\frac{1}{1000}$ mercuric chloride, whereas all the sodium thioglycolate broth subcultures showed growth. This test indicates that bichloride of mercury

THE ANTIBACTERIAL ACTION OF CERTAIN DISINFECTANTS

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FROM the time of Robert Koch it has been a commonly accepted belief that mercury bichloride is an efficient germicide for the destruction of bacterial spores as well as vegetative forms of microorganisms. More recently certain inorganic and numerous organic mercurial preparations have been popularized and widely employed as chemical disinfecting agents.

In spite of their popularity mercurial disinfectants have certain disadvantages. Bichloride of mercury is markedly toxic, irritating, and corrosive. Some of the newer mercurials and, especially, certain organic compounds show considerable improvement in these respects. The main defect of the mercurials, however, lies in their high bacteriostatic powers in comparison with their bactericidal abilities; they often prevent bacteria from multiplying without actually killing them. As a result of such bacteriostasis the mercurials tend to give falsely high phenol coefficient values and show spectacular results when tested by the agar cup plate technique.

The relatively high bacteriostatic and low bactericidal power of bichloride of mercury was first reported by Geppert (see Welch¹), in 1889, and was well recognized by Welch¹ and his co-workers as early as 1891. More recently it has become evident that the actual bactericidal or bacteria-killing powers of practically all mercurial disinfectants are remarkably low, a fact which was lately (1940) emphasized by a report of the Council of Pharmacy and Chemistry of the American Medical Association.² Brewer³ (1939) demonstrated that organic mercurial compounds cannot be relied upon for killing spores which may contaminate surgical and dental instruments, sutures and other materials. It is also easy to show with the use of sodium thioglycolate medium (Brewer⁴) that many mercurial disinfectants, in the concentrations customarily employed, are unable to kill certain nonspore-forming bacteria. The experiments here reported are mostly tests performed for the Los Angeles County Hospital on the bactericidal efficacies of certain mercurials in comparison with aqueous iodine plus potassium iodide and also with aqueous zephiran (Alba).

The following technique was employed for most of the experiments. Eighteen-hour broth cultures of *Staphylococcus aureus* and of *Escherichia coli* were used as test organisms. Various dilutions of the disinfectants were made in 5 c.c. volumes in distilled water. One-half cubic centimeter of a test culture was pipetted into 5 c.c. of each disinfectant, mixed and allowed to stand at room temperature. After five and ten minutes, subcultures were made with an approximately standard phenol coefficient loop into tubes containing about 10 c.c. of (a) plain broth and (b) sodium thioglycolate broth. These subcultures were incubated at 37° C. for a minimum of forty-eight hours and observed for growth. Random subcultures showing growth were stained by Gram's method and examined for contamination but no contamination was observed. Tables I and II are illustrative of the results obtained and represent experiments that were performed at the same time on the germicidal activities of aqueous iodine and mercuric chloride against *E. coli*.

TABLE I

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	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH
Full strength	-	-	-	-
$\frac{1}{4}$	-	-	-	-
$\frac{1}{16}$	-	-	-	-
$\frac{1}{64}$	-	-	-	-
$\frac{1}{256}$	+	-	+	+

+ = Growth
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TABLE II

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DILUTIONS OF $\frac{1}{1000}$ MERCURIC CHLORIDE	5-MINUTE SUBCULTURES		10-MINUTE SUBCULTURES	
	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH	PLAIN BROTH	SODIUM THIO- GLYCOLATE BROTH
Full strength	-	+	-	+
$\frac{1}{4}$	-	+	-	+
$\frac{1}{16}$	-	+	-	+
$\frac{1}{64}$	-	+	-	+
$\frac{1}{256}$	-	-	+	-

+ = Growth
- = No growth } of *E. coli* in ninety-six hours

Table I indicates that 1 per cent aqueous iodine in dilutions up through $\frac{1}{64}$ apparently killed the test organisms. No growth was observed in the subcultures made into plain broth or sodium thioglycolate broth until dilutions of aqueous iodine exceeding $\frac{1}{64}$ were tested. Table II shows a very contrasting picture. Subcultures into plain broth failed to grow until they were made from an original $\frac{1}{256}$ dilution of the $\frac{1}{1000}$ mercuric chloride, whereas all the sodium thioglycolate broth subcultures showed growth. This test indicates that bichloride of mercury

has a marked bacteriostatic rather than a bactericidal action. It inhibited growth by bacteriostasis in most of the plain broth subcultures but failed to do this in sodium thioglycolate broth. Many sulfur-containing compounds, and especially sodium thioglycolate, can neutralize the bacteriostatic action of mercurials and allow bacteria, which are inhibited but not killed, to multiply once more. It is of interest to consider in this connection that various sulfur-containing compounds are present in the human body. Aqueous iodine 1 per cent, in contrast to mercuric chloride, showed an apparent bactericidal effect in dilutions up through $\frac{1}{64}$ and its bacteriostatic action likewise disappeared above this point.

Table III summarizes all experiments on the disinfectants that were tested by the above methods. As a result of the use of sodium thioglycolate broth as one of the subculturing mediums, the effective germicidal strengths of the mercurials are shown to be surprisingly low although they would have appeared extremely efficacious if subcultures had been made only into plain broth.

TABLE III
SUMMARY OF DISINFECTANTS TESTED

DISINFECTANT	NUMBER OF EXPERI- MENTS	HIGHEST FINAL DILUTION OF DIS- INFECTANT WHICH PROVED EFFICACIOUS IN TEN MINUTES OF ACTION AT ROOM TEMPERATURE AGAINST	
		<i>Staph. aureus</i>	<i>E. coli</i>
Mercurials			
Mercurochrome (aqueous)	1	Less than $\frac{1}{20}$	Less than $\frac{1}{20}$
Mercuric chloride	1	Less than $\frac{1}{4000}$	Less than $\frac{1}{4000}$
*Phenylmercuric acetate (cystan)	4	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Tincture metaphen	1	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Merthiolate solution	1	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Tincture mercoseptic	1	$\frac{1}{4000}$	$\frac{1}{4000}$
Nonmercurials			
Aqueous iodine (plus double concentration of KI)	4	$\frac{1}{6400}$	$\frac{1}{6400}$
Zephiran (aqueous)	4	$\frac{1}{16,000}$	$\frac{1}{4000}$

*This is approximately four times the strength of cystan that is recommended by its manufacturer for the sterilization of cystoscopes and other instruments.

Prolonged contact with at least one of the mercurials at room temperature was shown to exert a bacteriostatic but no bactericidal effect. In three experiments, phenylmercuric acetate (cystan) was employed in the concentration recommended for cystoscope sterilization (approximately $\frac{1}{3800}$). *Staph. aureus* was left in contact with this disinfectant for periods ranging up to two and one-half hours. Subcultures into sodium thioglycolate broth showed luxuriant growth after the longest period of exposure, although the subcultures that were made into plain broth, at all intervals from five minutes to two and one-half hours, failed to grow.

Mercuric cyanide, $\frac{1}{1000}$, was tested in a different manner inasmuch as subcultures were made into blood broth and blood agar after varying periods of exposing *Staph. aureus* to this chemical. Staphylococcus colonies too numerous to count were observed in blood plates poured after exposures up to and including twenty-four hours and all the blood broth subculture tubes showed growth.

Zephiran and aqueous iodine have a number of advantages which will be noted briefly. Zephiran is but slightly toxic on intraperitoneal injection into mice; several normal mice tolerated $\frac{1}{1000}$ aqueous zephiran in doses of 0.01 c.c. per gram of body weight by the intraperitoneal route, although deaths were encountered when this dose was doubled. Aqueous zephiran, $\frac{1}{1000}$, appears to be practically nontoxic when taken by mouth. A mouse was given dry food with $\frac{1}{1000}$ aqueous zephiran as its only source of fluid for a period of two months; the mouse suffered no ill effects and was still living and well one month after the conclusion of this test. Aqueous zephiran is nonirritating to skin, has a low surface tension, and acts as a fairly efficient detergent. It is also relatively nonirritating to open wounds and to mucous membranes and is being used increasingly as a germicide for skin preparation and also for the irrigation of infected wounds, sinuses, and cavities. Zephiran seems also adapted for the chemical sterilization of instruments which cannot be exposed to heat. It evidently has little corrosive action other than that of the water in which it is dissolved. It was shown to have no deleterious effect upon the type of cement employed in cystoscopes. In one test a portion of a cystoscope was immersed for seventeen days at room temperature in $\frac{1}{1000}$ aqueous zephiran without the occurrence of any noticeable corrosion of the metal or injury to the cement. In order to minimize corrosion it has been recommended that 0.5 per cent sodium nitrite be added to aqueous zephiran when this disinfectant is used for the storage of metal instruments.

Both zephiran and aqueous iodine appear to have bactericidal powers, against the test organisms employed, in dilutions approximately as high as those showing bacteriostasis. Iodine, when improperly used, has and can cause severe burns. It is our opinion, however, that iodine could well be utilized for skin preparation in dilutions considerably higher than those commonly employed. This would minimize the chance of iodine burns and should still be effective. It has been shown that aqueous iodine, in concentrations that cause little irritation to tissues, can still act as an effective germicide. Salle and his associates,⁵ working with their "toxicity index" technique, compared a number of disinfectants and reported that aqueous iodine exhibited the least toxicity to tissues, relative to its bacteria-killing ability, of all disinfectants tested. Thompson, Isaacs, and Khorazo⁶ checked the action of various disinfectants against a strain of *Staph. aureus*, using the germicides in their maximum nonirritating concentrations as determined by instillation on the corneas

has a marked bacteriostatic rather than a bactericidal action. It inhibited growth by bacteriostasis in most of the plain broth subcultures but failed to do this in sodium thioglycolate broth. Many sulfur-containing compounds, and especially sodium thioglycolate, can neutralize the bacteriostatic action of mercurials and allow bacteria, which are inhibited but not killed, to multiply once more. It is of interest to consider in this connection that various sulfur-containing compounds are present in the human body. Aqueous iodine 1 per cent, in contrast to mercuric chloride, showed an apparent bactericidal effect in dilutions up through $\frac{1}{64}$ and its bacteriostatic action likewise disappeared above this point.

Table III summarizes all experiments on the disinfectants that were tested by the above methods. As a result of the use of sodium thioglycolate broth as one of the subculturing mediums, the effective germicidal strengths of the mercurials are shown to be surprisingly low although they would have appeared extremely efficacious if subcultures had been made only into plain broth.

TABLE III
SUMMARY OF DISINFECTANTS TESTED

DISINFECTANT	NUMBER OF EXPERI- MENTS	HIGHEST FINAL DILUTION OF DIS- INFECTANT WHICH PROVED EFFICACIOUS IN TEN MINUTES OF ACTION AT ROOM TEMPERATURE AGAINST	
		<i>Staph. aureus</i>	<i>E. coli</i>
Mercurials			
Mercurochrome (aqueous)	1	Less than $\frac{1}{20}$	Less than $\frac{1}{20}$
Mercuric chloride	1	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
*Phenylmercuric acetate (cystan)	4	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Tincture metaphen	1	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Merthiolate solution	1	Less than $\frac{1}{1000}$	Less than $\frac{1}{1000}$
Tincture mercoseptic	1	$\frac{1}{1000}$	$\frac{1}{4000}$
Nonmercurials			
Aqueous iodine (plus double concentration of KI)	4	$\frac{1}{6400}$	$\frac{1}{6400}$
Zephiran (aqueous)	4	$\frac{1}{16,000}$	$\frac{1}{4000}$

*This is approximately four times the strength of cystan that is recommended by its manufacturer for the sterilization of cystoscopes and other instruments.

Prolonged contact with at least one of the mercurials at room temperature was shown to exert a bacteriostatic but no bactericidal effect. In three experiments, phenylmercuric acetate (cystan) was employed in the concentration recommended for cystoscope sterilization (approximately $\frac{1}{3800}$). *Staph. aureus* was left in contact with this disinfectant for periods ranging up to two and one-half hours. Subcultures into sodium thioglycolate broth showed luxuriant growth after the longest period of exposure, although the subcultures that were made into plain broth, at all intervals from five minutes to two and one-half hours, failed to grow.

THE USE OF TANTALUM CLIPS FOR HEMOSTASIS IN NEUROSURGERY

ROBERT H. PUDENZ, M.D., MONTREAL, QUE.

(From the Department of Neurology and Neurosurgery of McGill University and the Montreal Neurological Institute.)

THE introduction of the silver clip by Harvey Cushing,⁴ in 1911, was a notable advance toward the solution of the problem of hemostasis in neurosurgery. Cushing's original silver clip outfit was considerably improved by McKenzie⁷ who changed from the round to a flattened silver ribbon and designed more efficient instruments for cutting, holding, and applying the clips. Penfield⁸ designed a smaller clip for use with the McKenzie apparatus (Fig. 1).⁹ This small clip is sizable enough for the control of bleeding from most cerebral vessels and, in addition, is admirably suited for neurosurgical procedures on experimental animals. As a result of the experiments described in this communication, we believe that a further change in the clip is justified, namely, the replacement of silver by tantalum.

The disadvantage of the silver clip lies not in its mechanical properties, but in the extensive inflammatory reaction which it produces in the surrounding tissues. This is a matter of common experience among neurosurgeons and neuropathologists. It has been repeatedly disclosed at a subsequent craniotomy or necropsy. Because of this reaction many neurosurgeons limit their use of silver clips, employing them only when other methods of hemostasis will not suffice.

It is surprising that reports of surgical complications attributable to silver clips are almost nonexistent in the literature. Thorner and Groff¹⁰ have described a case of bilateral lumbar posterior root irritation by migrating silver clips, which occurred four months after a negative suboccipital exploration for tumor. The presence of the clips at the points of emergence of the involved roots was confirmed by roentgenography. It is not unlikely that other complications have occurred but have been either unrecognized or unrecorded.

The neurosurgical staff of this hospital has long been interested in the development of an inert metal from which the Cushing clip could be fabricated. Several metals in current surgical use have been considered. Principal among these inert metals, in addition to tantalum, are vitallium and the several types of stainless steel.

Vitallium is an alloy containing 65 per cent cobalt, 30 per cent chromium, and 5 per cent molybdenum. The widespread use of this metal in surgery is attributable to the original and encouraging experimental findings of Venable, Stuck, and Beach.¹¹ Screws, nails, and

*As manufactured by the J. F. Hartz Co., Limited, of Montreal and Toronto, under Dr. McKenzie's supervision.

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of albino rabbits; they reported that zephiran showed the most marked and rapid disinfecting action and iodine also placed relatively high in this respect. Since iodine has the disadvantage of being corrosive to metals, it should not be employed routinely for the cold sterilization of instruments although it might serve as a valuable emergency sterilizing agent.

DISCUSSION

The ideal disinfectant for skin preparation, for the irrigation of infected wounds and cavities, and for the cold sterilization of instruments has not been demonstrated to date. Laboratory tests, such as those here reported, are mainly of value as an argument against the use of mercury-containing compounds which can easily be shown to have high bacteriostatic but low bactericidal powers. Aqueous iodine and zephiran both appear to possess high bactericidal powers as well as high bacteriostatic abilities; it is only fair to add, however, that any compound showing apparently high bactericidal powers may eventually be proved to act mainly by bacteriostasis provided that a proper subculturing medium, analogous to sodium thioglycolate for the mercurial compounds, can be developed. Iodine, when properly employed, would seem to be a valuable agent for skin preparation. Zephiran appears to show considerable promise for numerous uses as a disinfectant. It should be more widely tested, however, in order that its true values and limitations be thoroughly understood.

SUMMARY AND CONCLUSIONS

A number of mercurial disinfectants, which are commonly employed for skin preparation and for the cold "sterilization" of instruments, were tested for their relative bacteriostatic and bactericidal powers against *Staph. aureus* and *E. coli*. All mercurials tested were shown to have relatively high bacteriostatic abilities but low bactericidal powers. Aqueous iodine and zephiran, on the other hand, appeared to be highly bactericidal as well as bacteriostatic.

Certain properties and uses of aqueous iodine and zephiran are further discussed.

REFERENCES

1. Welch, W. H.: Papers and Addresses by William Henry Welch, Vol. II, Bacteriology, Baltimore, 1920, Johns Hopkins Press, pp. 412-417.
2. Report of the Council of Pharmacy and Chemistry of the American Medical Association, J. A. M. A. 115: 2083, 1940.
3. Brewer, J. H.: J. A. M. A. 112: 2009, 1939.
4. Brewer, J. H.: J. A. M. A. 115: 598, 1940.
5. Salle, A. J., McOmie, W. A., Sheehmeister, I. L., and Foord, D. C.: J. Bact. 37: 639, 1939.
6. Thompson, R., Isaacs, M. L., and Khorazo, D.: Am. J. Ophth. 20: 1087, 1937.

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plates of this material are routinely used by many surgeons in the open treatment of fractures. In addition, vitallium cups have been successfully employed for arthroplasty of the hip by Smith-Petersen.⁹ Geib⁵ has recently reported the satisfactory repair of cranial defects with this metal.

The orthopedic scope of the stainless steels is essentially similar to that of vitallium. These metals have a further surgical value as suture materials. Their popularity for this latter purpose is due largely to Babcock.¹

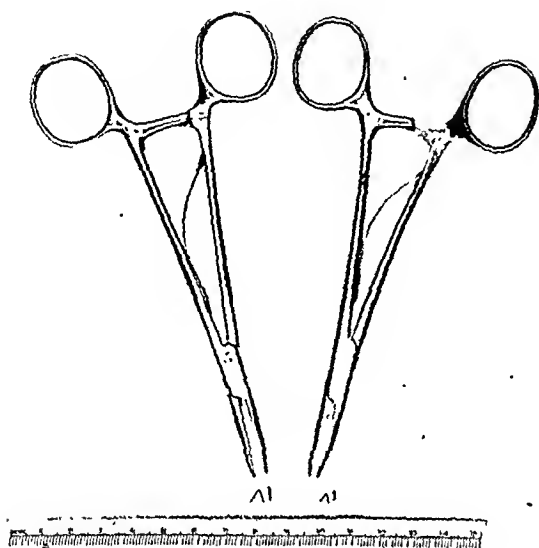


Fig. 1.—Forceps and clips for use with the McKenzie apparatus; Penfield's smaller modification is shown at the right.

Certain inconsistencies of results with these stainless steels have been attributed to variations of chemical composition. The alloy most extensively employed at the present time is the 18/8 type, so-called because it contains 18 to 20 per cent chromium and 8 to 10 per cent nickel. Key⁶ has recently introduced enduro, another variety of stainless steel. This alloy contains 16 to 20 per cent chromium, a maximum of 14 per cent nickel, and 2 to 4 per cent molybdenum. He has found experimentally that this alloy is more resistant to corrosion than the 18/8 type.

Unfortunately, vitallium is not adaptable for use in the McKenzie type of clip outfit. Vitallium appliances are made by casting. The alloy cannot be drawn into wire or rolled. It is, therefore, impractical for the manufacture of a thin ribbon from which hemostatic clips could be cut. In contrast, the various types of stainless steel can be cold rolled, drawn into wire, and tempered to varying degrees of hardness. Stainless steel surgical wire does not have the dead-soft

anneal comparable to silver in its plasticity. However, the use of these alloys for the Cushing clip is a matter for further investigation.

The difficulties associated with the search for a metal having the plastic mechanical properties of silver and, in addition, the quality of inertness in the tissues, have been obviated since the recent introduction of tantalum.

In contrast to vitallium and the stainless steels, tantalum is not an alloy but an element, the seventy-third in the periodic table. It was discovered in 1802, by Ekeberg, who so named it because of his "tantalizing" experiences on attempting to dissolve the metal in mineral acids. Physically it is a blue-gray, heavy, malleable, and ductile metal. Chemically it approaches glass in its resistance to acids. Only hydrofluoric and sulfuric acids will attack it. While resistant to weak alkalis, it is destroyed by boiling alkalis and the salts which hydrolyze to form strong alkalis.

Theoretically, these characteristics allow the conclusion that tantalum would be inert in the physicochemical environment of animal tissue. That this is actually so has been shown by the researches of Burch and Carney² and Burke.³ These observers have used tantalum sutures, bone plates, and screws in both animal and human tissues. In none of their subsequent exposures was there evidence of tissue irritation or corrosion of the metal. The screws became so firmly embedded in the bone that they were removed with difficulty. Burke reports that in his series of thirty-four patients, in whom tantalum was used for skin closure, there was a striking absence of scar tissue at the site of skin penetration.

The encouraging results obtained by these observers led to this experimental comparison of the reaction provoked by tantalum and silver in the brain and meninges of animals. In view of the short periods of observation, the report may be criticized as being premature. Nevertheless, it is hoped that the encouraging results obtained in these experiments will stimulate further investigation of the surgical value of this metal.

EXPERIMENTAL COMPARISON OF TANTALUM AND SILVER CLIPS

Adult cats, anesthetized with intraperitoneal nembutal in doses of 40 mg. per kilogram, were used for the experiments. Under aseptic conditions the cerebral hemispheres were exposed bilaterally through single trephine openings. The dura was incised in a cruciate manner and the leptomeninges perforated with the point of a scalpel at the proposed site of insertion of the metallic strips.

Strips of tantalum and silver ribbon, identical in all dimensions, were used. These strips were 0.75 inch in length, 0.030 inch in width, and 0.020 inch in thickness. Each strip was angulated 90 degrees to an "L" shape resulting in a longer and shorter arm measuring 0.5 and 0.25 inch respectively.

plates of this material are routinely used by many surgeons in the open treatment of fractures. In addition, vitallium cups have been successfully employed for arthroplasty of the hip by Smith-Petersen.⁹ Geib⁶ has recently reported the satisfactory repair of cranial defects with this metal.

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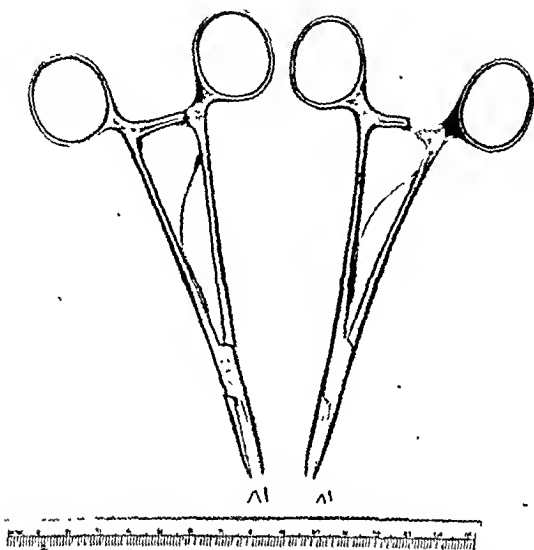


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capsule was greater in the later stages following implantation. It was firmly bound to the overlying dura. The extracted silver clip had a brownish-black discoloration of its surface. Finally, on cutting the tract of the clip in cross section, a marginal zone of greenish softening, at times 3 mm. in diameter, was noted (Fig. 3).

In contrast, the tantalum ribbon provoked but minimal reaction. Encapsulation of the meningeal segment was at most a delicate, translucent membrane continuous with the leptomeninges. Meningocerebral adhesions at the site of insertion were few and fragile. The blue-gray luster of the metal was unchanged. The tract, as seen in cross section, was sharply outlined. Reaction in the surrounding brain was indiscernible with the naked eye (Fig. 3).

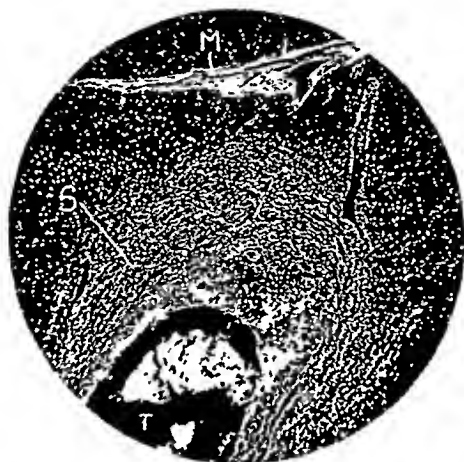


Fig. 4A.—Reaction surrounding silver clip thirty days after implantation. Note the large masses of polymorphonuclear leucocytes within the tract (T), the secondary zone (S) of glial, vascular, and connective tissue response and the extension of the reaction into the leptomeninges of an adjacent sulcus (M).

Microscopic Findings.—The gross impression of the intensity of the reaction surrounding the silver clip was confirmed by microscopic examination. For practical purposes this reaction is divisible into proximal and distal zones. In the early stages the proximal zone consisted of a wide collar of polymorphonuclear leucocytes. Later many of these cells showed degenerative changes with small round cells and phagocytes filled with brown-black pigment granules dispersed among them. Surrounding this area of compact cells was the distal zone in which chromatolysis of ganglion cells, amoeboid types of microglia, gliosis, and the proliferation of blood vessels were noted. The term "gliosis" is used broadly to indicate the proliferation and hypertrophy of astrocytes with the laying down of neuroglia fibrils. Collections of small round cells and compound granular corpuseles were found around the vessels. The distal zone was the large number of fibroblasts.

The longer arms of these angulated strips were inserted perpendicularly into the cerebral hemisphere, the shorter arm lying in contact with the pia-arachnoid (Fig. 2). The tantalum strips were placed in the right, the silver in the left, cerebral hemispheres. The dural flaps were replaced but not sutured. The temporalis muscles, galea, and skin were approximated with interrupted sutures of black silk and a dry dressing was applied.



Fig. 2.—Diagrammatic cross section of brain showing position of tantalum (T) and silver (S) strips, the shorter arm of the strip rests on the pia-arachnoid while the longer arm extends into the depths of the cerebral hemisphere.



Fig. 3.—Tracts of the tantalum (T) and silver (S) ribbons in the right and left frontal lobes after eleven days. The area of reaction around the silver strip is obvious (magnification $\times 4$).

Eleven cats were used for this study. The animals were killed at intervals varying from 10 to 148 days. Prior to removal, the brain was fixed in situ by internal carotid perfusion with animal Ringer's solution followed by 10 per cent formalin. The removed brain, with dura intact, was placed in 10 per cent formalin.

When properly hardened the dura was reflected from the cortical surface and the site of strip implantation examined for reaction. Following this inspection the strips were carefully withdrawn from the brain. Blocks of cerebral tissue for microscopic study were cut in a plane allowing examination of the tract of the metal in cross section. These blocks were further hardened in 10 per cent formalin, embedded in paraffin and sectioned at $10\ \mu$. The sections were stained by the hematoxylin and Van Gieson, the Mallory phosphotungstic acid hematoxylin, the Cajal gold chloride sublimate, and the Hortega silver carbonate methods.

RESULTS

Gross Findings.—The meningeal arm of the silver clip was invariably embedded in a mass of tough, pearly tissue. The thickness of this

refinement in technique. Large and small tantalum hemostatic clips for use in the McKenzie clip forceps are now in routine use in our operating theatres. The large clips are cut from dead-soft annealed tantalum ribbon 0.028 inch wide by 0.014 inch thick, and the small clips from a ribbon 0.020 inch wide by 0.010 inch thick. These ribbons are narrower in both dimensions than the standard silver ribbons and are not knurled. The tantalum clips are similar to silver clips in plasticity and permit a firm grasp on the site of hemorrhage.

Further studies of the neurosurgical value of tantalum are now in progress. The metal has been used in the form of a foil to protect cerebral wounds from the ingrowth of dural fibrous tissue and tantalum sheet of varying thickness has been employed to obliterate bony defects in the skull. The results of these experiments will be published in a later communication.

SUMMARY AND CONCLUSIONS

1. The reactions provoked by silver and by tantalum ribbon when implanted in the brains and meninges of cats for periods of time varying from 10 to 148 days are reported.

2. The silver clip provokes an intense inflammatory reaction in both nervous tissue and meninges, leading eventually to dense encapsulation.

3. The reaction to tantalum consists of a minimal investment by connective tissue and/or neuroglia fibrils. The characteristic foreign body reaction is not found.

4. The conclusion drawn from this evidence is that the tantalum clip should replace the silver clip for hemostasis in neurosurgical procedures. This is particularly true in cases where irritation leading to focal epilepsy may be feared as a late complication of operation.

The tantalum ribbon used in these experiments was supplied through the courtesy of the Fansteel Metallurgical Corporation of North Chicago, Ill.

REFERENCES

1. Babcock, W. W.: Catgut Allergy; With a Note on the Use of Alloy Steel Wire for Sutures and Ligatures, *Am. J. Surg.* 27: 67-70, 1935.
2. Burch, J. C., and Carney, H. M.: Personal communication.
3. Burke, G.: The Corrosion of Metals in Tissues: And an Introduction to Tantalum, *Canad. M. A. J.* 43: 125-128, 1940.
4. Cushing, H.: The Control of Bleeding in Operations for Brain Tumors With the Description of Silver "Clips" for the Occlusion of Vessels Inaccessible to the Ligature, *Ann. Surg.* 54: 1-19, 1911.
5. Geib, F. W.: Vitallium Skull Plates, *J. A. M. A.* 117: 8-12, 1941.
6. Key, J. A.: Stainless Steel and Vitallium in Internal Fixation of Bone; a Comparison, *Arch. Surg.* 43: 615-626, 1941.
7. McKenzie, K. G.: Some Minor Modifications of Harvey Cushing's Silver Clip Outfit, *Surg., Gynec. & Obst.* 45: 549-550, 1927.
8. Penfield, W. G.: Unpublished data.
9. Smith-Petersen, M. N.: Arthroplasty of the Hip; a New Method, *J. Bone & Joint Surg.* 21: 269-288, 1939.
10. Thorner, M. W., and Groff, R. A.: An Unusual Complication Following Suboccipital Craniotomy, *Surgey* 4: 434-437, 1938.
11. Venable, C. S., Stuck, W. G. and Beach, A.: The effects on Bone of the Presence of Metals: Based Upon Electrolysis, *Ann. Surg.* 105: 917-938, 1937.

These cells eventually formed a thick sheath of collagenous connective tissue around the metal. These proximal and distal zones of reaction are evident in Fig. 4, *A*. In this instance the inflammatory cells have extended into the leptomeninges of an adjacent sulcus.

Examination of the brain bordering the tantalum tract disclosed but slight reaction to this metal. Mobilization of inflammatory cells and the proliferation of fibroblasts and vessels were minimal. At the end of 148 days the strip was invested in a thin collagen sheath bordered by a narrow zone of astrocytic proliferation and hypertrophy. In a few instances compound granular corpuscles filled with blood pigment were noted in the tract. The presence of these cells was undoubtedly the result of hemorrhage concurrent with insertion of the strips. In one experiment, where the strip lay partly within a sulcus, the meningeal component of the tract consisted of a narrow, collagenous band while the cerebral component was the usual neuroglial brushwork. The characteristic reaction to tantalum is shown in Fig. 4, *B*.

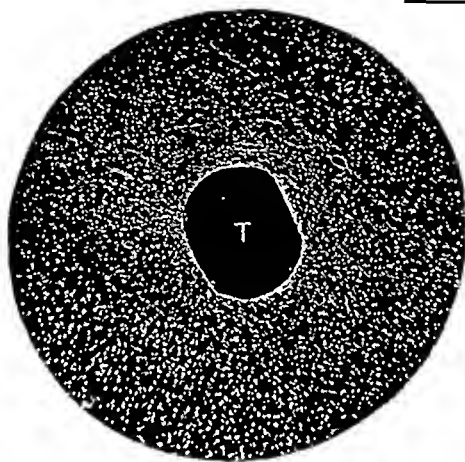


Fig. 4*B*.—Cross section of tract (*T*) occupied by tantalum for thirty days; note the slight marginal gliosis and the lack of inflammatory reaction.

DISCUSSION

These findings offer additional evidence that tantalum does not irritate tissues. In all of the experiments the reaction to the metal, when in contact with the meninges or nervous tissue, was a minimal encapsulation by fibroblasts and/or neuroglia fibrils, depending on the location. In contrast, silver has invariably provoked an intense inflammatory reaction, leading ultimately to investment in dense collagenous connective tissue. The character of this tissue reaction to silver is not unlike that of cerebral abscess formation.

In view of the intensity of the reaction to silver, we are convinced that the replacement of this metal by tantalum is a considerable

ulceration is still unestablished. However, it poses as an interesting speculative problem. We have previously expressed the belief that all patients with gastroduodenal ulceration are potential candidates for perforation but only those ulcers perforate which are exposed to certain precipitating "perforative" factors. These consist essentially of trauma, infection, and a local lack of tissue resistance.

There are still other interesting, controversial, and incompletely understood problems in the pathology, bacteriology, clinical manifestations, and diagnosis of perforated gastroduodenal ulceration but their consideration here would be inopportune and inexpedient. More pertinent are the prognostic and therapeutic considerations. Thus, although the mortality in this condition has steadily decreased during the first three decades of the present century, it has diminished almost insignificantly during the last decade. This poor reflection of considered improvement in diagnostic methods, preoperative and postoperative therapy, anesthesia, and surgical technique clearly emphasizes the necessity for a more intensive consideration of this subject.

There are a number of prognostically influential factors in this complication. Among the most important of these are sex, age, location of the lesion, time elapsing between perforation and treatment, type of anesthetic employed, and development of complications. It is an interesting and unsatisfactorily explained fact that the mortality in females is almost twice that in males. More readily explicable is the significance of the age factor, which is shown by the fact that in patients under 40 years of age the mortality is less than 20 per cent, whereas in those over 40 years there is a commensurate increase in mortality from 30 to 50 per cent. The prognostic significance of the site of perforation is demonstrated by the fact that the mortality is from 10 to 15 per cent greater in gastric than in duodenal perforations. This has been explained on the basis that the former are more liable to occur in older patients and are more liable to be associated with greater spillage of intragastric contents into the peritoneal cavity. It has long been common knowledge that the mortality in perforated ulcer is almost directly proportional to the time elapsing between the perforation and the operation, that is, the longer this period the greater the mortality. This is clearly demonstrated by the fact that in an analysis of more than 7,000 cases, the mortality in those treated during the first six postperforative hours was about 10 per cent, whereas in the second six-hour period the mortality doubled, in the third quadrupled, and in the fourth had increased sixfold. Although the importance of anesthesia is somewhat controversial, the majority of recent observers consider spinal analgesia the most desirable. The fact that the mortality following spinal analgesia was approximately one-half that following general anesthesia in a large collected series clearly emphasized its significance. We have previously expressed the opinion that the former is preferable because complete relaxation is obtained, permit-

Editorial

Acute Perforated Gastroduodenal Ulceration

PROBABLY the most frequent and the most serious complication of gastroduodenal ulceration is acute perforation. On the basis of large statistical studies it has been estimated that from 10 to 15 per cent of all "peptic" ulcers perforate and that from 20 to 25 per cent of all patients with perforated ulcer die. Even more significant is the fact that this complication is apparently increasing. Moreover, it would not be hazardous to predict that with the present wide-flung conflict there will be an even greater increase in the incidence of acute perforation. The cause of this increase has not been explained satisfactorily but a number of psychic and physical factors are believed to be contributory. Included among these are economic strain, poor nutrition, accelerated mental and physical activities, excessive smoking and imbibition of alcoholic beverages, and, particularly in soldiers, nostalgia, mental depression, and other emotional stresses. Accordingly, if these factors play significant roles in the development of gastroduodenal ulceration, and there is good reason to believe that they do, current military operations on such a prodigious scale will undoubtedly be associated with an even greater increase in the incidence of this serious complication.

There are a number of other interesting features of acute gastroduodenal perforation that are not thoroughly understood. Thus, it has long been known that from 90 to 95 per cent of these complications occur in males, and almost three-fourths of the patients are between the ages of twenty and fifty years. The possibility of a "protective" or hormonal factor obviously suggests itself as an explanation for the sexual predominance but in spite of isolated studies this remains in the intriguing speculative phase. Similarly, the relative immunity in individuals under twenty years of age remains conjectural. Whereas some significance has been attributed to a racial factor, careful observers have shown that this condition occurs with almost equal frequency among Caucasian, Negroid, and Asiatic races. Similarly, the existence of a seasonal influence remains disputative. The etiologic significance of occupation in perforated ulcer also is not clear. Whereas it is commonly believed that the high tensioned, energetic executive is the most liable candidate for this complication, extensive statistical analyses have shown that the laboring classes comprise the largest number.

Another intriguing question is: Why do ulcers perforate? This is obviously difficult to answer because the etiology of gastroduodenal

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE PHYSIOLOGY OF PLASMA PROTHROMBIN AND ITS RELATION TO LIVER FUNCTION*

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INTRODUCTION

THE consideration of the plasma prothrombin in modern surgery had its inception approximately ten years ago when Lewisohn,¹ while studying the clotting mechanism in the hemorrhagic tendency associated with jaundice, found that the level of plasma prothrombin was reduced. However, the direct connection between lowered levels of plasma prothrombin and the hemorrhagic tendency associated with jaundice was not appreciated until 1935, when Quick, Stanley-Brown, and Baneroff² observed a definite relationship between the occurrence of hemorrhage and lowered levels of plasma prothrombin as indicated by a satisfactory test devised by Quick.^{3, 4} The use of this test and others, in particular the titration method of Warner, Brinkhous and Smith,⁵ has added much to our knowledge of the physiology of plasma prothrombin, including the establishment of the site of its formation and loss, its fluctuations in a variety of physiologic and pathologic states, and its relation to vitamin K.

It was early established that the liver is intimately related to plasma prothrombin, and as further information accumulated various workers have utilized the level of activity of this substance as a measure of hepatic function.

NATURE OF PLASMA PROTHROMBIN

A. Chemical Studies.—Brinkhous⁶ recently described the following characteristics of plasma prothrombin. It is associated with the pseudoglobulin fraction of the plasma protein, is salted out of plasma between one-third and one-half saturation with ammonium sulphate and at pH 5.3 is largely precipitated from diluted plasma. Prothrombin is also precipitated by adding acetone to plasma and is nondialyzable through collodion and cellophane. It is adsorbed on a number of colloidal preparations, including calcium phosphate, magnesium hydroxide, aluminum

*This study was carried out under a grant from the John and Mary R. Markle Foundation.

ting better exposure and less manipulative trauma, and because the toxicity of the latter is an additional burden upon the liver.

Although all are agreed that the treatment of acute perforated gastroduodenal ulceration is surgical, there is considerable controversy regarding the procedure of choice; the majority of American and English surgeons favor the more conservative procedure of simple closure and the continental European surgeons warmly advocate the more radical procedure of partial gastrectomy. Between these two extremes lie the advocates of closure plus gastroenterostomy and excision plus closure or pyloroplasty. The attempt to determine the superiority of these respective procedures by the comparative mortality rates is fallacious because numerous other factors such as those already mentioned, as well as the personal equation of the skill and experience of the surgeon, influence the mortality. Indeed, such a statistical study revealed that the mortality following the more conservative procedure of simple closure was not only the highest but twice as great as that following the more radical procedure of gastrectomy. This obvious discrepancy with well-established surgical principles clearly emphasizes the importance of other factors. That the various procedures advocated have their respective advantages, disadvantages, and indications is readily admitted and has been comprehensively reviewed in a previous publication. However, on the basis of surgical rationale, it is our firm conviction that the procedure of choice in the majority of cases is the one which effects most expeditiously adequate repair of the defect. Accordingly, the procedure of simple closure is considered the most desirable. Reinforcement with an omental graft is of additional value. Of interest in this connection and for the sake of recorded accuracy it should be realized that the use of an omental plug was suggested in 1896 by Bennett. The procedure of added gastroenterostomy in the majority of cases is considered not only unnecessary and "meddlesome" surgery but also hazardous because of the subsequent development of an anastomotic jejunal ulcer. Whereas the reported incidence of this serious complication varies from less than 5 to over 50 per cent, depending upon the care and thoroughness of the follow-up studies, we are convinced that it occurs with sufficient frequency and associated danger to justify its condemnation. In fact, its one occasional justification, pyloric constriction, may be combated better by some form of pyloroplasty.

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hydroxide, and colloidal starch, as well as by passing plasma through a Seitz filter. It is thermolabile, being destroyed by heating plasma for one-half hour at 56° C. Preservation of plasma at room temperature leads to fairly rapid disintegration of prothrombin, whereas plasma in the frozen state maintains its prothrombin activity for weeks. Biologically potent but chemically crude preparations of prothrombin have been prepared by Mellanby,⁷ and by Seegers, Smith, Warner, and Brinkhous,⁸ by precipitation from dilute plasma at pH 5.3 and adsorption on magnesium hydroxide. It is then separated from the adsorbing agent by carbon dioxide and dialyzed against water to remove a number of insoluble impurities. After evaporation the resultant dry powder is water soluble, and contains approximately 150 units of prothrombin per milligram. Brinkhous adds that a more recent preparation of prothrombin by modification of the above method has yielded a substance having a potency of 500 units per mgm.

B. *Biologic Activity*.—Although the exact chemical nature of prothrombin remains an unsolved mystery, its biologic activity has been established during the past seven years, as involved in the clotting mechanism as follows:

1. Prothrombin + calcium + thromboplastin → thrombin
2. Thrombin + fibrinogen → fibrin (clot)

Eagle⁹ concludes that calcium and thromboplastin are catalysts which speed the conversion of the prothrombin to thrombin and that thrombin is likewise a catalytic agent which activates the transformation of fibrinogen to fibrin reaction. In Eagle's studies on snake venom and various enzymes such as trypsin, the basic two stages could be carried out without calcium and thromboplastin in the first process and thrombin in the second process. However, Mertz, Seegers, and Smith¹⁰ believe that thromboplastin is not an enzyme but rather that it takes part in the reaction and therefore suggest that the first stage is a direct chemical interaction in which both thromboplastin and prothrombin are consumed.

C. *Tests for Plasma Prothrombin*.—Tests for plasma prothrombin merely assay its capacity to form thrombin and its activity is assumed to parallel the amount present.

Quick's test^{3, 4} is a one-stage technique for measuring the clotting time of oxalated plasma after the addition of an excess of thromboplastin and a relatively optimal amount of calcium. The assumptions are made that the fibrinogen is normal and that the clotting time which ensues represents the amount of prothrombin present. Actually, two temporal components exist, the time for the conversion of prothrombin to thrombin, and the time it takes the thrombin to act on the fibrinogen.

The Warner, Brinkhous, and Smith⁸ test, on the other hand, is a two-stage technique which allows for the conversion of the prothrombin

to thrombin and then with a fixed amount of fibrinogen, calcium, and thromboplastin the time required for the clot to occur is determined. The amount of thrombin formed is equivalent to the quantity of prothrombin present and the solution is diluted so that when the second stage is carried out a clot will form in fifteen seconds. A unit of thrombin is defined as the quantity which, under standard conditions, will cause clotting of 1 c.c. of a fibrinogen solution in fifteen seconds. One unit of prothrombin is the amount required to form one unit of thrombin. By this test, human plasma contains approximately 300 units of prothrombin per c.c.

Allen, Julian, and Dragstedt¹¹ described a modification of the Quick test which is more sensitive in the detection of hypoprothrombinemic states and more accurately depicts the response in the plasma prothrombin to therapy with vitamin K. Their modification consists in the serial dilution of the plasma, to concentrations ranging from fifty to five per cent of the original undiluted plasma. The authors used thromboplastin made from lung extract, and normal human plasma as a control with each group of unknowns.

More recently Ziffren, Owen, Hoffman, and Smith¹² described a so-called "bedside test" for prothrombin activity in which freshly drawn whole blood is mixed with a fixed amount of thromboplastin and the clotting time determined. All patients are checked with a control and the result is expressed in per cent of normal. The authors have found that for practical purposes there is a fairly close parallel between the level of plasma prothrombin as determined by the "bedside test" and the two-stage titration technique.

Kato¹³ in 1940 described a microprothrombin test which is a modification of Quick's test and in which oxalated whole capillary blood is used instead of larger amounts of venous plasma. It requires only 10 c.mm. of whole blood, and hence has great applicability in studies of plasma prothrombin in infants.

Ferguson, Calder, and Reinhold¹⁴ compared Quick's test with the serum volume test of Boyce and McFetridge¹⁵ and with the bleeding time of Ivy¹⁶ on a group of patients and found that the latter two tests used in conjunction never failed to detect a potential or actual bleeder due to prothrombin deficiency.

SOURCE OF PLASMA PROTHROMBIN

A. *Experimental Studies.*—Earlier speculation had suggested the bone marrow as the source of plasma prothrombin.¹⁷ Barnes,¹⁸ however, demonstrated in laboratory animals (mouse, rat, rabbit, and dog) that depression of the bone marrow by large doses of roentgen rays in acute experiments, as well as by protracted courses of small doses of x-ray, had no effect on the level of the plasma prothrombin. The true

site of its formation was indicated by Smith, Warner, and Brinkhous¹⁹ who, using chloroform as the hepatotoxin, observed a precipitous fall in plasma prothrombin to less than 10 per cent within twenty-four hours, and a return to normal only after six days had elapsed. Quick⁴ made similar observations on the dog, with chloroform anesthesia.

Warner,²⁰ after removing approximately 65 per cent of the liver of the rat, demonstrated a fall in plasma prothrombin which returned to normal in about two and one-half weeks. Andrus, Lord, and Moore,²¹ and Warren and Rhoads²² independently performed total hepatectomy in dogs and found that the plasma prothrombin fell progressively to lower levels. The former workers also demonstrated that the administration of vitamin K in large amounts failed to alter this rate of fall, indicating that the liver is the chief, if indeed it is not the sole site of prothrombin formation. Recently, Brinkhous and Warner²³ found that the plasma prothrombin depressed by chloroform poisoning failed to respond to vitamin K therapy.

Bollman, Butt, and Snell²⁴ produced chronic hepatic injury in the rat with carbon tetrachloride vapor and were able to demonstrate depression of the plasma prothrombin level and failure of vitamin K to influence it. These authors also observed that a high carbohydrate diet delayed the onset of hepatic damage and prolonged the lives of the animals by as much as 50 per cent.

B. Clinical Studies.—Many observers during the past four years have stressed the fact that in the presence of hepatic disease the plasma prothrombin not only is depressed but also fails to respond adequately to vitamin K therapy. Quick,⁴ Butt, Snell, and Osterberg,²⁵ Brinkhous, Smith, and Warner,²⁶ Stewart and Rourke,²⁷ Rhoads,²⁸ Lucia and Aggeler,²⁹ Pohle and Stewart,³⁰ Allen and Julian,³¹ and Andrus and Lord³² reported cases in which poor response was obtained and attributed this to liver damage.

Although there is some variation in the above authors' opinions as to the exact types of hepatic disease in which the plasma prothrombin fails to respond to the administration of vitamin K, there is general agreement that vitamin K therapy is adversely influenced by the presence of hepatic damage and that improvement in hepatic function is usually associated with a rise in the plasma prothrombin.

DESTRUCTION OF PLASMA PROTHROMBIN

Andrus, Lord, and Kauer³³ have pointed out that plasma prothrombin is being continuously lost from the blood as it circulates through the lungs. In a series of twenty experiments the prothrombin activity was found to be less in the blood of the left ventricle than in that from the right ventricle in seventeen. This difference averaged 10.6 per cent and ranged from 4 to 19 per cent. In no instance was the level in the

right ventricle lower than that in the left. In samples of blood taken from the arterial and venous supply of the head, liver, spleen, intestine, kidneys, and lower limbs no significant difference in plasma prothrombin levels was found. A possible explanation of this role of the lung in the loss of plasma prothrombin was thought to be the production of blood platelets in this organ. Platelets, as they undergo disintegration, initiate the first stage of the clotting process by releasing thromboplastin, which, in the presence of calcium, changes prothrombin to thrombin.

The importance of the above finding is to substantiate further the fact that plasma prothrombin is biologically a highly labile substance and any injury to the liver, its source, is followed by a fall in the amount in circulation in a very short period of time.

TESTS OF LIVER FUNCTION

A. Plasma Prothrombin as an Index of Hepatic Function.—The vital role played by the liver in the formation of prothrombin and the rapidity with which the level of this substance falls after experimental liver injury or hepatectomy suggest the possibility of following the level of the plasma prothrombin as an index of liver function. Pohle and Stewart³⁰ in 1940, were the first to publish a report of clinical experience with such a test, suggesting specifically that the response of a depressed plasma prothrombin level as measured by the Quick test, to vitamin K and bile salts administered by mouth, might be a satisfactory means of indicating liver function. In their series of 46 jaundiced patients with reduced plasma prothrombin, 28 showed a satisfactory response, while in 18 there was no improvement. Wilson (34) also suggested that the level of the plasma prothrombin might be considered as an index of hepatic function, and in a series of 36 patients found a close correlation between the level per se and the results of hippuric acid tests.

The use of the level of the plasma prothrombin alone as a measure of liver function is open to serious objection, however, since it may be depressed by dietary or other factors in the absence of liver damage.

Since October, 1939, we have studied the application of the level of plasma prothrombin and its response to intramuscular 2-methyl-1, 4-naphthoquinone as a measure of liver function in some eighty-six cases, and within certain restrictions find it perhaps the most accurate method available. We prefer the parenteral route, intramuscular in all our own cases, for the reason that we have encountered at least two otherwise normal individuals in whom, despite the presence of bile in the intestine and apparently normal liver function by several tests, the plasma prothrombin was depressed to about 60 per cent of normal and could not be elevated by vitamin K administered by mouth with or without bile salts. Intramuscular injection was followed by a prompt elevation to normal. This we can only explain by postulating a defective absorption from the intestinal tract.

We therefore have adopted the thesis, which is well borne out by clinical data to be presented below, that the level of the plasma prothrombin if below 80 per cent in a given case, is an index of the performance of the liver, while the response to 2 mg. of 2-methyl-1, 4-naphthoquinone administered intramuscularly indicates whether any depression of this function is or is not due to organic liver disease.

B. Comparison of Tests for Hepatic Function.—During the past four years a large number of tests of hepatic function have been studied by a variety of workers and as a result have attained a useful place in the study of patients. The hippuric acid test, the galactose tolerance, bromsulphalein excretion, and Hanger's cephalin-cholesterol flocculation tests seem to be the outstanding ones in use at present.

The hippuric acid excretion test has been found of value in the preoperative evaluation of the surgical patient by Boyce and McFetridge,³⁵ and they have made use of the test in hyperthyroidism as have Bartels³⁶ and Haines, Magath and Power.³⁷ The consensus of opinion is that while the test cannot supplant clinical judgment in estimating the danger of thyroidectomy to the patient or in indicating the length of time preoperative preparation should be continued, it does emphasize that the liver is intimately concerned in the metabolic derangement of the patient with hyperthyroidism and may be involved in the production of the symptom of postoperative thyroid crisis.

Quick³⁸ advocates the hippuric acid test as a useful means of differentiating intrahepatic and extrahepatic jaundice, but Snell and Plunkett³⁹ concluded that the test was of less aid in the differentiation of the two types of jaundice, although they did consider it more satisfactory than the galactose tolerance and bromsulphalein excretion tests in the estimation of the degree of hepatic damage.

During the past two years several reports have been made on the comparison of the plasma prothrombin and the other liver function tests mentioned above, with the exception of the cephalin-cholesterol flocculation test.

Wilson⁴⁰ found in nonjaundiced patients with a wide variety of diseases of the liver, a close correlation between the level of the plasma prothrombin as measured by the two-stage titration test of Warner, Brinkhous, and Smith⁵ and the hippuric acid test described by Quick.³⁸ On the other hand, Lucia and Aggeler²⁹ concluded that there was no significant correlation between the two tests although they felt that the response of the plasma prothrombin to vitamin K reflects the state of the liver in a variety of diseases of the liver and biliary tract. These workers drew their conclusions from prothrombin determinations by the method of Quick,³ but as Wilson⁴⁰ pointed out, the margin of error in the Quick test is rather too large for such exact estimations. We agree with Lucia and Aggeler that the response of the plasma prothrombin to

vitamin K therapy is a better measure of liver function than the level of the prothrombin because of the relative frequency of conditions such as sprue, ulcerative colitis, etc., in which hepatic function is normal but the absorption of the vitamin is defective. We also agree with Wilson that the two-stage prothrombin test is essential in the exact determination of hepatic function and comparison with other tests. Kark, White, Souter, and Deutsch,⁴¹ using the Quick test for plasma prothrombin, found no significant correlation between the hippuric acid test and the response of the plasma prothrombin to synthetic vitamin K analogues. DeLor and Reinhart,⁴² comparing the plasma prothrombin as determined by the Quick test, bromsulphalein excretion, galactose tolerance, and hippuric acid tests, concluded that the bromsulphalein test is the most sensitive one of their series for the identification of early liver damage, and consider the galactose tolerance test the least reliable of the group. In all cases in which the hippuric acid excretion was below 2.0 Gm., the plasma prothrombin was reduced, while in the group whose excretion of hippuric acid was between 2.0 and 3.0 Gm., the plasma prothrombin was normal in 87 per cent of the cases.

Andrus and Lord⁴³ have employed the response of plasma prothrombin to intramuscular injection of menadione (2-methyl-1, 4-naphthoquinone) as determined by the Warner, Brinkhous, and Smith test as a measure of hepatic function and have compared the test with the galactose tolerance, hippuric acid, and bromsulphalein clearance tests in three groups of selected patients. In a group of seven patients with Laënnec's type of cirrhosis of the liver the plasma prothrombin failed to rise by more than 6 per cent after the intramuscular injection of 2 mg. of menadione. This failure to respond, we feel, indicates intrahepatic disease of a significant degree, but prognosis is only possible when the test is employed on several occasions and the trend observed. The galactose tolerance test was used in six of the seven patients with cirrhosis of the liver and results were abnormal in only four. The hippuric acid test was less accurate than the galactose tolerance test, being below 100 per cent (3 Gm.) in only two out of five of the cases. The bromsulphalein test stood last in point of accuracy with three normal results in three cases of cirrhosis.

In a group of nine cases of catarrhal jaundice the plasma prothrombin test showed impaired hepatic function in seven instances and in general paralleled the severity of the disease. The galactose tolerance test was equally accurate in this group, showing greater than 3 Gm. excreted in seven out of nine patients. The results in the hippuric acid test were abnormal in three out of seven cases, while those in the bromsulphalein test were abnormal in only two out of five instances. Interestingly, the bromsulphalein test gave abnormal results (10 per cent retained) in one case of catarrhal jaundice proved at operation, in which the results of the other three tests were normal.

We therefore have adopted the thesis, which is well borne out by clinical data to be presented below, that the level of the plasma prothrombin if below 80 per cent in a given case, is an index of the performance of the liver, while the response to 2 mg. of 2-methyl-1, 4-naphthoquinone administered intramuscularly indicates whether any depression of this function is or is not due to organic liver disease.

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plasma prothrombin with galactose tolerance and bromsulphalein clearance tests is of interest. They found that the plasma prothrombin fell to 28 per cent of normal in twenty-four hours after the injection of 0.12 c.c. per kilogram of chloroform, while the galactose tolerance test remained normal (less than 3.0 Gm. excreted). When 0.24 c.c. per kilogram of chloroform was injected, the plasma prothrombin fell to less than 3 per cent of normal, while the galactose tolerance test showed an excretion of only 3.6 Gm. in the urine. The bromsulphalein test with 0.03 c.c. per kilogram showed an average retention of 2 per cent in 30 minutes (up to 10 per cent retention is considered to be normal), while the plasma prothrombin fell to an average of 67 per cent. When 0.12 c.c. per kilogram of chloroform was used, the bromsulphalein showed a retention of 25 per cent, while the plasma prothrombin fell to 6 per cent.

It is evident from the above findings that the plasma prothrombin is a far more sensitive index of liver damage in chloroform intoxication than is the bromsulphalein clearance test, and that the latter is considerably more sensitive than the galactose tolerance test.

RELATION OF PLASMA PROTHROMBIN TO SURGICAL DISEASE

As a working hypothesis to be applied in any specific instance, we may look upon the vitamin K-plasma prothrombin relationship in the following way. Into the final formation of plasma prothrombin there enters an extrinsic factor, vitamin K; an intrinsic factor, bile salts; an absorptive mechanism, the intestinal epithelium; and the liver, which not only stores vitamin K but from it elaborates prothrombin.

Any derangement of function or lack of supply of any of the above factors may lead singly or in combination to lowered levels of plasma prothrombin, and hence to the hemorrhagic tendency now known to be associated with a wide range of pathologic states.

A. Obstructive Jaundice.—In this condition, whether it be due to carcinoma of the head of the pancreas, stone in the common duct, or some other pathologic abnormality blocking the biliary pathways, the bile is prevented from reaching the intestinal tract, with the result that the absorption of all fat-soluble vitamins, of which K is one, is interfered with. As this continues, the level of the hepatic store of the vitamin falls, and there is a concomitant fall in the plasma prothrombin. Lord, Andrus, and Moore⁴⁴ demonstrated by the curative method of assay on chickens that the liver of dogs made vitamin K deficient by exclusion of bile from the intestinal tract (obstructive jaundice or biliary fistula) contains progressively less vitamin K, and that the level of the plasma prothrombin bears a linear relationship to the quantity of the vitamin in the liver. In addition, if the obstruction continues unabated, morphologic changes in the liver occur which are characterized

The third group of patients studied suffered from obstructive (extra-hepatic) jaundice due to a variety of lesions. The plasma prothrombin response was good in all of eleven cases in which it was used, while the galactose tolerance test was normal in only six out of nine cases. The hippuric acid test was normal in seven out of eight and the bromsulphalein test was normal in all four cases in which it was used. In this group of patients with extrahepatic jaundice the question arises as to whether the impairment of hepatic function as determined by the galactose tolerance test is significant or not. If significant, then the plasma prothrombin test is less sensitive in this group than the galactose tolerance test. It seems clear that the bromsulphalein test was the least sensitive in each of the three groups of cases and that the plasma prothrombin is the most accurate, with the galactose tolerance test a close second. The hippuric acid test falls between the galactose tolerance and the bromsulphalein tests in point of accuracy.

TABLE I

COMPARATIVE RESULTS OF LIVER FUNCTION TESTS SHOWING GREATEST IMPAIRMENT 21 TO 48 HOURS AFTER MINIMAL DOSES OF CHLOROFORM

CHLOROFORM (C.C. PER KG.)	DOG NUMBER	PLASMA PROTHROMBIN PER CENT OF NORMAL (NORMAL = 100%)	BROMSULPHALEIN PER CENT RETAINED (NORMAL = 0.10%)	GALACTOSE TOLERANCE GRAMS EXCRETED (NORMAL = < 3.0 GM.)
0.03	1	70	0	
	2	69	7	
	3	62	0	
0.06	4	75	0	
	5	58	0	
0.09	6	60	0	
0.10	7	< 8	10	
	8	< 6	25	
0.12	9	< 3		2.9
	10	54		1.5
0.18	11	< 2		3.3
	12	< 3		3.2
0.24	13	< 3		3.9

< = less than

However, all clinical studies of the comparison of various liver function tests are unsatisfactory because of the difficulty in controlling the many factors which may influence the disease and the patient. Also, diagnosis cannot always be established with certainty without operation or autopsy. Hence, recent work by Andrus and Lord⁴³ on the use of the injection of minute amounts (0.03 to 0.24 c.c. per kilogram) of chloroform subcutaneously into dogs and comparing the level of the

plasma prothrombin with galaetose toleranee and bromsulphalein clearanee tests is of interest. They found that the plasma prothrombin fell to 28 per cent of normal in twenty-four hours after the injection of 0.12 c.c. per kilogram of ehloroform, while the galaetose toleranee test remained normal (less than 3.0 Gm. exereted). When 0.24 c.c. per kilogram of ehloroform was injected, the plasma prothrombin fell to less than 3 per cent of normal, while the galaetose toleranee test showed an exeretion of only 3.6 Gm. in the urine. The bromsulphalein test with 0.03 c.c. per kilogram showed an average retention of 2 per cent in 30 minutes (up to 10 per cent retention is considered to be normal), while the plasma prothrombin fell to an average of 67 per cent. When 0.12 c.c. per kilogram of ehloroform was used, the bromsulphalein showed a retention of 25 per cent, while the plasma prothrombin fell to 6 per cent.

It is evident from the above findings that the plasma prothrombin is a far more sensitive index of liver damage in ehloroform intoxication than is the bromsulphalein clearanee test, and that the latter is considerably more sensitive than the galaetose toleranee test.

RELATION OF PLASMA PROTHROMBIN TO SURGICAL DISEASE

As a working hypothesis to be applied in any specific instance, we may look upon the vitamin K-plasma prothrombin relationship in the following way. Into the final formation of plasma prothrombin there enters an extrinsic factor, vitamin K; an intrinsic factor, bile salts; an absorptive mechanism, the intestinal epithelium; and the liver, which not only stores vitamin K but from it elaborates prothrombin.

Any derangement of function or lack of supply of any of the above factors may lead singly or in combination to lowered levels of plasma prothrombin, and hence to the hemorrhagic tendency now known to be associated with a wide range of pathologic states.

A. Obstructive Jaundice.—In this condition, whether it be due to carcinoma of the head of the pancreas, stone in the common duct, or some other pathologic abnormality blocking the biliary pathways, the bile is prevented from reaching the intestinal tract, with the result that the absorption of all fat-soluble vitamins, of which K is one, is interfered with. As this continues, the level of the hepatic store of the vitamin falls, and there is a concomitant fall in the plasma prothrombin. Lord, Andrus, and Moore⁴⁴ demonstrated by the curative method of assay on chickens that the liver of dogs made vitamin K deficient by exclusion of bile from the intestinal tract (obstructive jaundice or biliary fistula) contains progressively less vitamin K, and that the level of the plasma prothrombin bears a linear relationship to the quantity of the vitamin in the liver. In addition, if the obstruction continues unabated, morphologic changes in the liver occur which are characterized

as obstructive biliary cirrhosis. This state of itself leads to a diminished capacity of the liver to elaborate plasma prothrombin even in the presence of an adequate supply of vitamin K. Hence, the patient with obstructive jaundice is likely to bleed if vitamin K with bile salts, orally, or menadione intramuscularly or intravenously are not administered, and if the disease progresses without relief to such an extent that the hepatic damage is too severe. In the former case therapeutic measures are effective, whereas in the latter all efforts to promote the formation of prothrombin may be in vain.

Before the advent of vitamin K, hemorrhage was the cause of death in approximately 50 per cent of the cases of obstructive jaundice in which patients died following surgical intervention. In contrast to the above findings, since the use of vitamin K there has been not a single death due to hemorrhagic tendency in patients with obstructive jaundice of extrahepatic origin on the surgical service of the New York Hospital.

It has been pointed out repeatedly in clinical studies that the hemorrhagic tendency more often becomes manifest in the postoperative period than at any other time. Stewart, Romke, and Allen⁴² found that the plasma prothrombin fell 15 to 25 per cent during the immediate postoperative period in a group of four patients subjected to operation upon the biliary tract, whereas the fall in the group of five patients without biliary tract disease was observed on only one case and amounted to only 15 per cent. We¹⁶ have confirmed the normal prothrombin levels in patients operated upon for brain lesions, hernioplasties, and major abdominal procedures in whom the liver was not handled. Lord⁴³ and Cullen and co-workers⁴⁴ have demonstrated in the dog that massage of the liver for twenty-five minutes produces a fall of 25 per cent in the level of the plasma prothrombin, from which recovery is made within six days. The latter workers have studied the effect of anesthesia on plasma prothrombin and found that of ether, cyclopropane, and chloroform, only the last produced significantly depressed levels during the postoperative period. Allen and Livingstone⁴⁵ studied a variety of anesthetic agents exclusive of chloroform and concluded that the postoperative fall which occurred was not due to the type of anesthetic but rather to the state of the stores of vitamin K, "potential prothrombin," in the body.

With the observation on the depressing effect of operation on the plasma prothrombin outlined above in mind, it would seem unwise to perform an elective operation on any patient with a level of plasma prothrombin below 50 per cent, as the critical bleeding level is 20 to 25 per cent of normal by the Warner, Brinkhous, and Smith test. Hence, allowing 25 per cent for the postoperative fall, there would be no margin for safety unless the plasma prothrombin were 50 per cent of normal or higher preoperatively.

Excellent clinical reports have been made by Smith and co-workers,⁵⁰ Butt, Snell, and Osterberg,²⁵ Dam and Glavind,⁵¹ Rhoads,⁵² Quick,⁴ Stewart and Rourke,²⁷ Illingworth,⁵³ and Allen and Julian.⁵⁴

B. Biliary Fistula.—The hemorrhagic tendency may become manifest in patients with a biliary fistula since, as in obstructive jaundice, the absence of bile in the intestine leads to a failure of the absorption of the fat-soluble vitamin K and hence to a diminished level of plasma prothrombin. Experimentally, Hawkins and Whipple⁵⁵ and Hawkins and Brinkhous⁵⁶ in 1935-1936 demonstrated the hemorrhagic tendency in dogs with biliary fistulae and showed that the bleeding was due to a deficiency of plasma prothrombin. The relation of vitamin K and the level of plasma prothrombin in dogs with biliary fistulae was determined by Smith, Warner, Brinkhous, and Seegers⁵⁷ in 1938. In these animals the liver remains normal grossly and microscopically and the fall in plasma prothrombin is more gradual than in the animals with obstructive jaundice, since in the latter the combination of exclusion of bile from the intestinal tract interfering with the absorption of vitamin K, and the mechanical obstruction to the outflow of bile may lead to a secondary hepatic damage in the form of cirrhosis.

Brinkhous, Smith, and Warner⁵⁶ in 1938 reported a case of external biliary fistula due to stricture of the common bile duct and observed plasma prothrombin levels of 29 per cent which, after the feeding of whole bile, rose to 89 per cent. There was temporary oozing of blood from the wound on the fourth and fifth postoperative days, which ceased following a blood transfusion. Zuckerman, Kogut, Jacobi and Cohen⁵⁸ in 1939 reported an excellent study of the plasma prothrombin and other hematologic findings in a patient with a complete external biliary fistula. The patient was placed on a low fat, vitamin K deficient diet without the administration of bile or bile salts, with the result that the plasma prothrombin time rose from 30 to 150 seconds and the patient bled from the gums, tongue, and vagina. Neither the prothrombin time nor the actual bleeding was altered by the feeding of bile or vitamin K alone, but the prothrombin time returned to normal (twenty seconds) and the bleeding ceased within eight days after the feeding of bile and vitamin K concentrate together. Numerous other workers have reported similar experiences.

C. Hepatic Disease.—Concomitantly with the development of the experimental evidence that the liver is the site of elaboration of plasma prothrombin, clinical studies revealed that prothrombin is lowered in a variety of diseases of the liver. Cirrhosis of the liver has been widely recognized to be associated with lowered levels of plasma prothrombin^{27, 34, 59, 60} and the failure of the plasma prothrombin to respond to vitamin K has been repeatedly emphasized by Allen and Julian,⁵⁴ Stewart,⁶¹ Andrus and Lord,³² and others. It is interesting to note that

in the authors' experience no case of extrahepatic jaundice has failed to respond to synthetic vitamin K therapy in spite of long-standing jaundice, of six months' duration in one case. On the other hand, only one case of typical cirrhosis has shown an elevation of plasma prothrombin following the injection of similar amounts of the vitamin.

Other types of liver disease such as multiple abscesses of the liver,⁶¹ catarrhal jaundice,^{61, 62} and subacute yellow atrophy⁶³ are associated with depressed levels of plasma prothrombin which fail to respond to vitamin K administration.

D. Intestinal Disease and Nutritional Deficiency.—Kark and Lozner,⁶⁴ using a modified Quick test, reported on changes in the prothrombin time in patients with simple nutritional deficiency of vitamin K. Their four patients were free from jaundice and intestinal and hepatic disease but did have signs of other vitamin deficiencies. On vitamin K concentrate without bile salts the prothrombin time, after having been markedly prolonged in the diluted plasmas, returned to normal within three days in all cases. Although these patients had hemorrhagic manifestations, it was the opinion of these authors that they were due to deficiency of vitamin C. Scarborough,⁶⁵ using Quick's test as a measure of plasma prothrombin, was unable to corroborate the finding of Kark and Lozner in patients with multiple vitamin deficiency. He concluded that the explanation of their different results lay in the different technique of determining plasma prothrombin. In spite of an adequate intake of vitamin K and a normal output of bile, certain patients with poor intestinal absorption such as may be seen in sprue, ulcerative colitis, etc., may have lowered levels of plasma prothrombin and in a few instances develop the hemorrhagic tendency. Clark and his co-workers,⁶⁶ in 1939, reported their experience with a wide variety of gastrointestinal diseases and associated hypoprothrombinemia. Stewart and Rourke⁶⁷ observed patients with chronic ulcerative colitis who had diminished levels of plasma prothrombin which responded to oral vitamin K therapy. MacKie⁶⁷ found low levels of plasma prothrombin in a wide variety of conditions not associated with jaundice or obvious hepatic disease. He reported in detail the findings in two cases of regional enteritis and two of ulcerative colitis, one case of Banti's syndrome and one case of tropical sprue complicated by chronic intestinal obstruction. In three of these cases there was severe hemorrhage and in all of them the plasma prothrombin time was prolonged.

We⁶² have followed quite by accident the plasma prothrombin in an interesting case of poor intestinal absorption of vitamin K in the absence of any clinical disease. The plasma prothrombin was determined at first as a control, and when the level of 52 per cent was found and repetition revealed this figure to be correct, careful studies were carried out to determine, if possible, the nature of the defect. Oral administra-

tions of 2 mg. of menadione produced no change in the level of the plasma prothrombin and similar failure of response followed menadione and bile salts in combination. However, intramuscular injection of 2 mg. of menadione produced a prompt elevation of the prothrombin which was maintained for one month. This patient has noted all her life an unusual tendency to bleed after minor trauma, dental operations, and tonsillectomy. Her diet has always been adequate in all respects. It would seem in this instance that we must postulate some defect of the intestinal absorptive mechanism.

E. Hemorrhagic Disease of Newborn.—In 1937, Brinkhous, Smith, and Warner⁶⁸ reported on the plasma prothrombin of newborn infants from the time of birth to ten and one-half months and observed extremely low levels during the first few days of life. Values ranging between 14 and 44 per cent of the adult normal were obtained and the normal level was approached by the age of ten and one-half months. Hellman and Shettles⁶⁹ confirmed the above findings and added that the levels of plasma prothrombin of premature infants were approximately one-third that of full-term infants, i.e., less than 10 per cent of the values of their mothers' prothrombin. Javert and Moore,⁷⁰ who employed the two-stage test of Warner, Brinkhous, and Smith, further confirmed these findings. In a series of twenty consecutive bloods taken at birth simultaneously from the cord and from the mother, the average level of the cord blood was 23 per cent and that of the mother 77 per cent.

Workers who have used the Quick prothrombin time as a measure of plasma prothrombin have obtained a variety of results from cord bloods. Quick and Grossman⁷¹ stated that the blood of infants three to seven days old was essentially the same as adults' blood. In a group of eight published cases the clotting time was within one-half second of the normal control in every instance. One month later Quick and Grossman⁷² reported three cases of cord blood with prothrombin levels of 71, 67, and 67 per cent, whereas in ten cases involving infants between the ages of six hours and two and one-half days the prothrombin percentage ranged between 80 and 7 per cent. In one instance the prothrombin rose from 15.5 per cent at the end of three and one-half days to 75 per cent at the end of five and one-half days. On the other hand, Norris and Rush⁷³ using the Quick test found that the prothrombin of cord blood in a series of fifty-one babies was 85 per cent and 63 per cent, depending on whether the plasma was undiluted or diluted with saline solution. Simultaneous determinations of the prothrombin of the mother's blood by the same technique revealed percentages of 117 and 140 respectively. Further confirmation of diminished levels of plasma prothrombin in newborn infants was added by Kato and Poncher,⁷⁴ who found in a series of 173 newborn infants average clotting times of 45 seconds on the first day

of life, 38 seconds on the second day, and a slower fall to 28 seconds by the twentieth day. Normal adult controls had clotting times averaging 20 seconds.

Waddell, Guerry, Bray, and Kelley,⁷³ who were the first to report on the effect of vitamin K on the plasma prothrombin of the newborn infant showed that there is a rapid and significant response in the prothrombin following oral administration of vitamin K concentrate. Shettles, Delfs, and Hellman⁷⁴ not only fed infants the vitamin but also observed the effect on the prothrombin of vitamin K administered to the mother before and during labor. This latter method produced an average elevation of plasma prothrombin in the infants to three times the normal controls.

Waddell and Guerry,⁷⁵ Nygaard,⁷⁶ Rhoads⁷² and others have recorded cases of hemorrhagic disease of the newborn with low levels of plasma prothrombin.

Recently Maumenee, Hellman, and Shettles⁷⁷ studied the retina of newborn babies and found that those with retinal hemorrhage showed lower levels of prothrombin than normal infants and that administration of vitamin K to mothers prior to the onset of labor almost entirely eliminated retinal hemorrhage in their infants.

There has been much speculation about the underlying physiology of the hypoprothrombinemia of the newborn, its further fall during the first few days of life, and its elevation from the eighth to tenth day. It is Quick's opinion that infants are born with a normal level of plasma prothrombin and develop a fall in this substance during the first forty-eight hours of life due to the fact that there is no reserve of prothrombin in the fetus and to the physiologic strain put on the infant during the first few days of life.

The recovery of the plasma prothrombin which Quick has found to occur abruptly in the second week of life he believes is due to bacterial synthesis of vitamin K in the intestinal tract of the infants with subsequent absorption and utilization by the liver for the elaboration of plasma prothrombin.

Tocantins⁸⁰ studied an infant with a complete septum between the first and second portions of the duodenum in whom the bile duct connected with the distal bowel, with the result that no food could get to the intestine although a normal amount of bile was present. Clinically the infant became jaundiced on the second day of life, vomited all food, passed meconium by rectum, and showed evidence of prolonged bleeding from a skin puncture. The plasma prothrombin was less than 1 per cent of normal. By the eleventh day of life the jaundice began to clear, bile was passed by rectum, and the plasma prothrombin rose to 113 per cent of normal. Tocantins concluded from the above case that bacterial activity in the intestine with subsequent formation of vitamin K was not

the underlying mechanism in the elaboration of the plasma prothrombin during the second week of life but rather that the true mechanism lay in the implied impairment of hepatic function of the newborn infant as evidenced by the analogous condition of "physiologic" icterus of the newborn.

A possible criticism of the above hypothesis may be found in the fact that the plasma prothrombin response to vitamin K in the newborn compares favorably with that of the adult in whom normal liver function is present. If impairment of liver function in the newborn is the underlying mechanism of the hypoprothrombinemia, there should be little or no response to vitamin K so long as such impairment exists.

Javert and Moore⁷⁰ postulated that since the circulation of the blood of the fetus from the placenta to the heart circumvents the liver via the ductus venosus by as much as 80 per cent of its volume, the plasma prothrombin of the blood in the peripheral circulation should be greatly reduced. Andrus and Lord⁸¹ constructed an Eek fistula in four dogs and observed a slow but steady fall in the plasma prothrombin to an average of 59 per cent of normal in an average of forty-three days. On the other hand, in three dogs with a reverse Eek fistula the plasma prothrombin averaged 89 per cent of normal at the end of an average of fifty-one days. In an Eek fistula the blood flow from the portal vein is shunted through the inferior vena cava and does not reach the liver due to ligation on the portal vein on the hepatic side of the anastomosis between the portal vein and the inferior vena cava. In the reverse Eek fistula the inferior vena cava is ligated cephalad to the anastomosis of the portal vein and the inferior vena cava and hence all the blood from the hind legs and pelvis pass through the liver along the portal flow.

From a therapeutic point of view it would seem best to treat all mothers just prior to or during labor with menadione and to administer the vitamin to the newborn infants if the level of prothrombin is low or if the infant should need any surgical procedure. On the pediatric service of the New York Hospital three infants have been observed who, following an episode of diarrhea, developed hemorrhagic manifestations associated with low levels of plasma prothrombin.⁸²

F. *Hyperthyroidism*.—For many years it has been pointed out that the liver is altered anatomically and functionally in the hyperthyroid patient. Weller,⁸³ Beaver and Pemberton,⁸⁴ and Shaffer⁸⁵ demonstrated that a wide variety of pathologic changes occur in the livers of patients with toxic goiter and that these range from widespread acute necrosis (usually central) to chronic patchy parenchymatous interlobular hepatitis. Functional impairment of the liver has also been noted, and Boyce and McPetridge,⁸⁶ Bartels and Perkin,⁸⁷ and Haines, Magath, and Power⁸⁸ have reported carefully studied series of patients, concluding that in general the higher the basal metabolic rate the poorer the

hepatic function as indicated by the hippuric acid excretion test, and that there is usually a significant depression in hepatic function after operation. Crile,⁸⁵ using the bromsulphalein excretion test, found that impairment of hepatic function in the postoperative course of relatively sick patients was most marked in elderly individuals with long-standing hyperthyroidism. It is his opinion that the delayed (third to seventh postoperative day) reaction of confusion, delirium, jaundice, and bronchopneumonia occasionally seen in elderly patients who have had severe hyperthyroidism is a possible terminal event due to hepatic insufficiency.

We⁸⁶ have studied a group of thirty-six cases of toxic diffuse and toxic nodular goiter and found that the level of plasma prothrombin shows little or no correlation with the preoperative basal metabolic rate, age or sex of the patient, or with the duration of the disease. On the other hand, it appeared that there was a marked fall in the plasma prothrombin during the immediate postoperative period, averaging 15 per cent but amounting to 40 per cent or more in some cases. The lowered levels were seen soon after operation and the normal level was attained only after one week had elapsed. The curves are quite similar to those obtained with chloroform anesthesia in patients as reported by Cullen, Ziffren, Gibson and Smith.⁴⁸ In one patient who developed clinical jaundice (icteric index, 50) following a first stage hemithyroidectomy, the plasma prothrombin fell from a preoperative level of 61 per cent to 43 per cent of normal on the first day and to 28 per cent on the third day after operation. Subsequent rise to 60 per cent of normal had occurred by the sixth day.

The above findings bring further important evidence to bear on the role of the liver in the patient with toxic goiter and it would seem highly advisable to use every means at hand to improve the patient's hepatic function during both the preoperative period of preparation and the immediate postoperative phase.

LIVER FUNCTION TESTS IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE

A wide variety of tests of liver function have been employed in an attempt to differentiate extrahepatic from intrahepatic jaundice but only a few of them have withstood rigid clinical application. There follows a comparison of the findings of those which have yielded the most accurate results.

A. Galactose Tolerance Test.—The galactose tolerance test was utilized by Shay and Schloss⁸⁹ and Schiff and Senior⁹⁰ with excellent results, being almost uniformly successful in the differentiation of the two groups of jaundice. On the contrary, Banks, Sprague, and Snell⁹¹ found that the test was of no real value when used as a differential diagnostic aid. Recently Bassett, Althausen, and Coltrin⁹² have brought forth a modification in the form of a galactose clearance test which appears to

provide a high degree of accuracy. They found that 82 per cent of a group of patients with obstructive jaundice of less than six months' duration had galactose clearance levels of less than 20 mg. per cent, while 81 per cent of the cases with idiopathic parenchymatous jaundice had more than 20 mg. per cent of galactose remaining in the blood seventy-five minutes after injection of 1 c.c. of a 50 per cent solution per kilogram. It would seem, however, that this overlap, although statistically small, may cause some limitation in the interpretation of the test in any given case of jaundice which presents a diagnostic problem.

B. Cephalin-Cholesterol Flocculation Test.—The other test to receive high recommendation in the differential diagnosis of jaundice is the cephalin-cholesterol flocculation test of Hanger.⁹³ In the hands of the author this test obtained an accuracy of 92 per cent, being correct in 58 out of 63 cases. Rosenberg⁹⁴ confirmed the findings of Hanger and made the observation that early in the course of jaundice a strongly positive flocculation test was indicative of an intrahepatic origin (8 out of 8 cases), whereas a negative or faintly positive test was suggestive of an extrahepatic cause for the jaundice. In 1 case out of 11 with obstructive jaundice a strongly positive test was obtained. On the other hand, Pohle and Stewart⁹⁵ found that the cephalin-cholesterol flocculation test is not satisfactory in the differential diagnosis of jaundice, although it is of marked sensitivity in the recognition of hepatic damage. In a series of twenty-three patients with obstructive jaundice, strongly positive (3+ and 4+) reactions were obtained in six instances. The duration of the jaundice in these six cases varied from two weeks to fourteen months, and the etiology of the obstruction included both malignant and benign causes for the extrahepatic block.

C. The Level of Plasma Prothrombin and Its Response to Menadione.

—Lord and Andrus⁶² have reported on the use of the response of the plasma prothrombin to intramuscular injection of menadione as a diagnostic aid in the differentiation of intrahepatic from extrahepatic jaundice. In a series of thirty-six cases of jaundice of intrahepatic origin the test was correct thirty-two times. In the group of extrahepatic jaundice it was correct in 49 cases out of 50. Hence, in a total of eighty-six cases where the test was applied, an accuracy of 94 per cent was attained. It is worth mentioning that there have been more than twenty cases of extrahepatic jaundice not included in the above group during the past year and a half in which the initial prothrombin was 80 per cent or more. We have found that every case of jaundice with an initial level of plasma prothrombin at 80 per cent or higher is one of extrahepatic origin. The technique of the test is to determine the level of plasma prothrombin on two successive days by the Warner, Brinkhous, and Smith test,⁵ and if the two levels are within 5 per cent of each other, 2 mg. of menadione are injected intramuscularly and the prothrombin

is determined at intervals of twenty-four, forty-eight, and seventy-two hours. On the other hand, if there is a difference greater than 5 per cent in the two initial levels of prothrombin, the level is determined on the third day, and so on, until the levels on two successive days are found to be within 5 per cent of each other. When such agreement occurs, then the menadione is administered. On no occasion have we found it necessary to determine the prothrombin for more than three successive days before injecting menadione.

Simultaneously and independently Allen and Julian²¹ reported on twelve cases of hepatic disease in which the response of the plasma prothrombin to the oral administration of menadione was sluggish or absent. They conclude, "that patients with chronic disease of the liver showed the most marked failure to respond to therapy. This, we believe, offers a characteristic of valuable diagnostic importance, in that failure of prothrombin response to adequate vitamin K in cases of jaundice would imply intrahepatic disease rather than obstruction of the bile ducts as the cause of the jaundice." Examination of their chart of twelve cases shows one patient with acute hepatitis and marked icterus who had an initial plasma prothrombin level of 41 per cent of normal, but which rose to 68 per cent after three days of treatment and to 95 per cent on the seventh day. This response, although not quite as rapid as is the typical case of extrahepatic jaundice, is at variance with our experience in which no case with catarrhal jaundice or acute hepatitis rose more than 29 per cent, and in the one case that rose by this amount a second trial of the test some two weeks later showed a fall of 9 per cent.

Recently, Olwin⁶³ confirmed the results of Lord and Andrus, and of Allen and Julian, except for the fact that he obtained a good response in the group of patients with catarrhal jaundice, and a failure to respond only in those patients with subacute yellow atrophy of the liver. Olwin and Lord and Andrus used the Warner, Brinkhous, and Smith test, while Allen and co-workers used their modification of the Quick test.¹¹

THERAPY OF PROTHROMBIN DEFICIENCY

From the above discussion of the metabolism of vitamin K, its relation to the intestinal absorptive mechanism and the role of the liver in the elaboration of plasma prothrombin, it becomes clear that there are several factors in the treatment of hypoprothrombinemia. At present prothrombin as such can be administered only in the form of blood transfusion as no concentrate of this substance has been described for clinical use. However, a transfusion is only a temporary therapeutic measure. The administration of vitamin K is a vital factor and this can be given in a variety of forms and by several different routes. Finally, and perhaps of greatest importance in the therapy of hypo-

prothrombinemia, is the maintenance of adequate liver function as no amount of vitamin K will elevate the plasma prothrombin in the presence of a severely damaged liver.

A. *Blood Transfusion*.—Judd, Snell, and Hoerner⁹⁶ pointed out the value of a transfusion of blood in the hemorrhagic state associated with obstructive jaundice and though of transient effect, found that a transfusion a few hours before operation might prevent serious hemorrhage subsequently. Experimental evidence demonstrating the effect of blood transfusion in the hemorrhagic state was presented by Smith, Warner, Brinkhous, and Seegers.⁵⁷ They showed that the plasma prothrombin was elevated and hemorrhage controlled when a transfusion of blood was carried out in a dog with a cholecystnephrostomy and a markedly depressed level of plasma prothrombin. The improvement was of temporary duration and hemorrhage recurred in a few days.

From a clinical study Stewart⁹⁷ suggested that a 600 c.c. transfusion of blood elevated the plasma prothrombin approximately 6 per cent. In controlled experiments in the dog Lord, Andrus, and Moore⁹⁸ demonstrated that the change in the total content of prothrombin in the plasma of a recipient after a transfusion was dependent on the prothrombin content of the plasma of the donor and may be calculated on the basis of addition.

There has been much controversy on the question of efficacy of "bank blood" as a source of plasma prothrombin ever since the original paper by Rhoads and Panzer⁹⁹ who found that the prothrombin level of bank blood by Quick's method rapidly declined to less than 25 per cent of normal during the first seven days of storage. Lord and Pastore¹⁰⁰ were the first to report on the levels of plasma prothrombin in bank blood as measured by the Warner, Brinkhous, and Smith test and found that rather than declining rapidly as observed by Rhoads and Panzer, the plasma prothrombin remained above 80 per cent of normal during the first week of storage and fell to 61 per cent by the end of the third week. Using the Quick test on the same samples of blood, Lord and Pastore confirmed the findings of Rhoads and Panzer. Subsequently, Warner, Dettowin, and Seegers¹⁰¹ confirmed the findings of Lord and Pastore when the Warner, Brinkhous, and Smith test was used, but did not observe a significant fall with the Quick test. However, Ziegler, Osterberg, and Hovig,¹⁰² employing both tests, observed a slow, gradual fall in plasma prothrombin with each test (an average of 75 per cent in four days, 65 per cent in eight days, and 40 per cent in thirty-seven days), and Quick, using his own test confirmed the findings of Rhoads and Panzer, and Lord and Pastore when the Quick test was used. Numerous other reports have been made but there is complete agreement in only one fact, namely, that the plasma prothrombin remains above 70 per cent of normal during the first five to seven days of

storage when determined by the Warner, Brinkhous, and Smith test, indicating that bank blood less than one week old is an adequate source of plasma prothrombin.

B. Vitamin K.—Originally, crude concentrates of alfalfa, fish meal, and spinach were employed as the source of vitamin K. With these several authors reported on the successful control of the hemorrhagic diathesis associated with jaundice and biliary fistula and of hemorrhagic disease of the newborn.^{25-27, 51, 68}

With the discovery that 2-methyl-1, 4-naphthoquinone and its derivatives were highly active antihemorrhagic substances and that they could be administered not only orally but also intramuscularly and intravenously, the therapy of hypoprothrombinemia was vastly improved. In addition, the role of the liver and of the intestinal absorptive mechanism became more clearly understood.

Intravenous administration of phthiocol by Bntt, Snell, and Osterberg¹⁰⁴ and Smith, Ziffren, Owen, and Hoffman⁵⁰ was described in 1939 and both groups of workers observed excellent responses in the plasma prothrombin to this synthetic substance. Synthetic vitamin K₁ was used intravenously by Frank, Hurwitz, and Seligman¹⁰⁵ with prompt and prolonged effect in two patients with hypoprothrombinemia. MacFie, Bacharach, and Chance¹⁰⁶ were the first to describe the intramuscular injection of 2-methyl-1, 4-naphthoquinone, and with the use of 10 mg. doses observed significant elevation of the plasma prothrombin. Andrus and Lord³² shortly thereafter confirmed the value of the intramuscular injection of 2-methyl-1, 4-naphthoquinone, obtaining excellent responses to 2 mg. doses in the absence of severe liver damage.

Rhoads and Fliegelman¹⁰⁷ reported the effectiveness of the oral administration of 2-methyl-1, 4-naphthoquinone in a group of ten patients. Shettles, Delfs, and Hellman⁷⁶ fed 2-methyl-1, 4 naphthoquinone to mothers in labor and to infants, and found it effective in elevating the plasma prothrombin.

The intravenous use of administration of other derivatives of naphthoquinone has been stressed by Olwin⁶³ as an ideal means of controlling hypoprothrombinemia. Both Olwin and Lord and Andrus have found parenteral routes for the administration of the synthetic vitamin K best for the differential diagnosis of jaundice.

Whether menadione is administered intravenously or intramuscularly, the effect on elevation of the plasma prothrombin is prompt (in 2 to 8 hours), significant (15 to 60 per cent rise in the absence of liver damage), and prolonged (7 to 20 days). Since in the parenteral use of vitamin K, bile salts are not necessary and the state of the intestinal absorptive mechanism and the presence of vomiting are of no consequence, there would seem to be little choice in the mode and route of

administration. Menadione should be used intramuscularly or intravenously in 2 mg. amounts every three to ten days, depending on the level of the plasma prothrombin. If there is no available means for determining the level of plasma prothrombin, then the injections should be carried out every three to four days until the basic condition (obstructive jaundice, biliary fistula, etc.) is rectified.

C. The Protection of the Liver.—During the past twenty-eight years factors which protect the liver from injury have been worked out on the experimental animal and subsequently applied to human needs. Thus, Opie and Alford¹⁰⁸ demonstrated the value of high carbohydrate diet in the protection of the liver of the rat against chloroform intoxication and also emphasized the ill effects of fat in the diet. This work has been repeatedly confirmed, but recently Johnson and his co-workers¹⁰⁹ observed that the proportion of fat in the liver was of more significance in the susceptibility of the liver to injury than the amount of glycogen present. It had been demonstrated earlier¹¹⁰ that a high fat diet was harmful to the liver of the dog when carbon tetrachloride was used as the hepatotoxin, animals on a high fat diet living only three weeks, in contrast to similar animals which on a high carbohydrate diet lived three to four months.

There has been little or no dispute over the fact that a diet high in carbohydrate and low in fat was best for the damaged liver, but there has been considerable controversy over the relation of protein in the diet. Bollman and Mann¹¹⁰ claimed that a diet of meat protein was harmful to dogs fed carbon tetrachloride and that in some of these dogs the survival period was considerably shorter than in the group fed a high carbohydrate diet. They felt that it was not the protein per se, but rather some water soluble substances of meat which were harmful, and hence that milk was a perfectly safe and adequate source of protein. Lord, Andrus, and Moore¹¹¹ confirmed the efficacy of a diet high in carbohydrate, low in fat, with milk as the source of protein in dogs with obstructive jaundice, demonstrating that animals on this carefully controlled diet lived on the average of seventy-five days, in contrast to a group of dogs which lived forty-seven days (an average) when kept on the regular balanced laboratory diet.

Recently, however, Messinger and Hawkins,¹¹² employing intravenous arsphenamine as the hepatotoxin found that a high protein diet (meat in the form of hamburger) protected the liver more effectively than any other diet. To quote from their paper: "in our experiments, the dogs with severe liver injury showed marked improvement when the diet was changed to protein, and there was not the slightest evidence that the meat diet was in any way injurious."

Johnson and his co-workers¹⁰⁹ demonstrated in dogs with the common a diet high in protein and carbohydrate with no fat

was more effective than the usual high carbohydrate diet in reducing the fatty acid concentration of the liver and in increasing the hepatic glycogen. This they have also confirmed in patients.

During the past three years experimental necrosis and cirrhosis of the liver have been produced in the rat¹¹² and rabbit¹¹³ using special diets which were deficient chiefly in the B complex. Rich and Hamilton¹¹³ found that rabbits fed a diet adequate in every respect except for the B complex developed cirrhosis of the liver in from 25 to 113 days. If all of the known synthetic vitamins of the B complex were added (thiamine, nicotinic acid, riboflavin, and B₆), the cirrhosis still occurred. However, if whole brewer's yeast was administered, the changes in the liver were prevented. Daft, Sebrell, and Lillie¹¹⁴ were able to produce cirrhosis of the liver in rats on a special diet and could prevent it by adding casein (30 per cent of the diet), methionine (0.7 per cent of the diet), or choline (20 mg. daily) either singly or in combination.

Drill and Hays,¹¹⁵ from a different viewpoint, demonstrated the value of whole brewer's yeast in maintaining normal liver function in the dog, as measured by the bromsulphalein test, when thyroid extract was administered.

Andrus and Lord¹¹⁶ have found that a minute amount of chloroform (0.12 c.c. per kilogram) when injected subcutaneously in the dog regularly produces a fall in the plasma prothrombin to 50 per cent of normal in twenty-four hours and that this fall is not recovered from until one week has elapsed. The range of fall of the plasma prothrombin varies in individual dogs from 73 to 2 per cent of normal, but the mean average is approximately 50 per cent. However, when whole brewer's yeast is administered in 1 Gm. per kilogram doses for from two to three days preceding the administration of the hepatotoxin, the fall of plasma prothrombin is cut in half and the period of recovery shortened to from four to five days.

Studies of some of the individual factors in the B complex reveal that thiamin, riboflavin, and nicotinic acid have no effect whatsoever in preventing the fall of plasma prothrombin after the test dose of chloroform. On the other hand, choline chloride in 200 mg. per kilogram doses for three days prevented the fall in the plasma prothrombin to a degree equal that of brewer's yeast. Because of the remarkable effect of brewer's yeast and of choline in protecting the liver from the action of chloroform, it would seem wise to include these substances in the diet of all patients with potential or actual damage to the liver.

The effect of anoxemia in producing hepatic damage has been demonstrated¹¹⁷ and should be borne in mind in selecting the anesthetic agent in patients with diminished liver function. Anemia, because of the anoxic effect it may have on the cells of the liver, should be corrected.

REFERENCES

1. Lewisohn, R.: Haematologic Studies as Basis for Determining Risk of Post-Operative Haemorrhage in Jaundice Patients, *Ann. Surg.* 94: 80, 1931.
2. Quick, A. J., Stanley-Brown, M., and Baneroff, F. W.: Study of the Coagulation Defect in Hemophilia and in Jaundice, *Am. J. M. Sc.* 190: 501, 1935.
3. Quick, A. J.: On Various Properties of Thromboplastin (Aqueous Tissue Extracts), *Am. J. Physiol.* 114: 282, 1936.
4. Quick, A. J.: Nature of the Bleeding in Jaundice, *J. A. M. A.* 110: 1658, 1938.
5. Warner, E. D., Brinkhous, K. M., and Smith, H. P.: Quantitative Study on Blood Clotting: Prothrombin Fluctuations Under Experimental Conditions, *Am. J. Physiol.* 114: 667, 1936.
6. Brinkhous, K. M.: Plasma Prothrombin; Vitamin K, *Medicine* 19: 329, 1940.
7. Mellanby, J.: Prothrombase—Its Preparation and Properties, *Proc. Roy. Soc., London*, s.B. 107: 271, 1930.
8. Seegers, W. H., Smith, H. P., Warner, E. D., and Brinkhous, K. M.: Purification of Prothrombin, *J. Biol. Chem.* 123: 751, 1938.
9. Eagle, H.: Recent Advances in the Blood Coagulation Problem, *Medicine* 16: 95, 1937.
10. Mertz, E. T., Seegers, W. H., and Smith, H. P.: Prothrombin, Thromboplastin and Thrombin: Quantitative Interrelationships, *Proc. Soc. Exper. Biol. & Med.* 42: 604, 1939.
11. Allen, J. G., Julian, O. C., and Dragstedt, L. R.: Use of Serial Dilutions in Determination of Prothrombin by the One Stage Technique, *Arch. Surg.* 41: 873, 1940.
12. Ziffren, P. E., Owen, C. A., Hoffman, G. R., and Smith, H. P.: Control of Vitamin K Therapy. Compensatory Mechanisms at Low Prothrombin Levels, *Proc. Soc. Exper. Biol. & Med.* 40: 595, 1939.
13. Kato, K.: Microprothrombin Test With the Use of Capillary Whole Blood: A Simplified Modification of Quick's Quantitative Method, *Am. J. Clin. Path.* 10: 147, 1940.
14. Ferguson, L. K., Calder, D. G., and Reinhold, J. G.: The Ivy Bleeding Time, Serum Volume Index and Prothrombin Content of Blood in Estimating Bleeding Tendency in Jaundice, *Surg., Gynec. & Obst.* 71: 603, 1940.
15. Boyce, F. F., and McFetridge, E. M.: Serum Volume Test for Hemorrhagic Diathesis in Jaundice, *J. Lab. & Clin. Med.* 23: 202, 1937.
16. Ivy, A. C., Shapiro, P. F., and Melnick, P.: Bleeding Tendency in Jaundice, *Surg., Gynec. & Obst.* 60: 781, 1935.
17. Wöhlisch, E.: Die Physiologie und Pathologie der Blutgerinnung, *Ergebn. d. Physiol.* 28: 443, 1929.
18. Barnes, W. A.: Prothrombin Formation Following Injury of Bone Marrow by Roentgen Rays, *Am. J. Roentgenol.* 46: 356, 1941.
19. Smith, H. P., Warner, E. D., and Brinkhous, K. M.: Prothrombin Deficiency and the Bleeding Tendency in Liver Injury (Chloroform Intoxication), *J. Exper. Med.* 66: 801, 1937.
20. Warner, E. D.: Plasma Prothrombin. Effect of Partial Hepatectomy, *J. Exper. Med.* 68: 831, 1938.
21. Andrus, W. DeW., Lord, J. W., Jr., and Moore, R. A.: Effect of Hepatectomy on the Plasma Prothrombin and the Utilization of Vitamin K, *SURGERY* 6: 899, 1939.
22. Warren, R., and Rhoads, J. E.: Hepatic Origin of the Plasma-Prothrombin Observation After Total Hepatectomy in the Dog, *Am. J. M. Sc.* 198: 193, 1939.
23. Brinkhous, K. M., and Warner, E. D.: Effect of Vitamin K on Hypoprothrombinemia of Experimental Liver Injury, *Proc. Soc. Exper. Biol. & Med.* 44: 609, 1940.
24. Bollman, J. L., Butt, H. R., and Snell, A. M.: Influence of Liver on Utilization of Vitamin K, *J. A. M. A.* 115: 1087, 1940.
25. Butt, H. R., Snell, A. M., and Osterberg, A. E.: The Preoperative and Post-operative Administration of Vitamin K to Patients Having Jaundice, *J. A. M. A.* 113: 383, 1939.

26. Brinkhous, K. M., Smith, H. P., and Warner, T. D.: Prothrombin Deficiency and the Bleeding Tendency in Obstructive Jaundice and in Biliary Fistula Effect of Feeding Bile and Alfalfa (Vitamin K), *Am J. M. Sc* 196: 50, 1938.
27. Stewart, J. D., and Rourke, G. M.: Prothrombin and Vitamin K Therapy, *New England J. Med* 221: 403, 1939.
28. Rhoads, J. D.: Physiologic Factors Regulating the Level of the Plasma Prothrombin, *Tr. Am. S. A.* 58: 86, 1940.
29. Lucin, S. P., and Aggeler, P. M.: The Influence of Liver Damage on the Plasma Prothrombin Concentration and the Response to Vitamin K, *Am J. M. Sc.* 201: 326, 1941.
30. Pohle, I. J., and Stewart, J. K.: Observations on Plasma Prothrombin and Effects of Vitamin K in Patients With Liver or Biliary Tract Disease, *J. Clin. Investigation* 19: 365, 1940.
31. Allen, J. G., and Julian, O. C.: Response of Plasma Prothrombin to Vitamin K Substitute Therapy in Cases of Hepatic Disease, *Arch. Surg.* 41: 1363, 1940.
32. Andrus, W. DeW., and Lord, J. W., Jr.: Correction of Prothrombin Deficiencies by Means of 2 Methyl 1, 4 Naphthoquinone Injected Intramuscularly, *J. A. M. A.* 114: 1336, 1940.
33. Andrus, W. DeW., Lord, J. W., Jr., and Kaufer, J. T.: Studies on the Fate of Plasma Prothrombin, *Science* 91: 48, 1940.
34. Wilson, S. J.: Quantitative Prothrombin and Hippuric Acid Determinations as Sensitive Reflection of Liver Damage in Humans, *Proc. Soc. Exper. Biol. & Med.* 41: 559, 1939.
35. Boyce, I. F., and McPetridge, E. M.: Studies of Hepatic Function by Quick Hippuric Acid Test Biliary and Hepatic Disease, *Arch. Surg.* 37: 401, 1938.
36. Bartels, E. C.: Liver Function in Hyperthyroidism as Determined by Hippuric Acid Test, *Ann. Int. Med.* 12: 652, 1938.
37. Haines, S. P., Magath, T. B., and Power, M. H.: Hippuric Acid Test in Hyperthyroidism, *Ann. Int. Med.* 14: 1225, 1941.
38. Quick, A. J.: Clinical Value of Test for Hippuric Acid in Cases of Disease of Liver, *Arch. Int. Med.* 57: 544, 1936.
39. Snell, A. M., and Plunkett, J. E.: The Hippuric Acid Test for Hepatic Function Its Relation to Other Tests in General Use, *Am. J. Digest. Dis. & Nutrition* 2: 716, 1936.
40. Wilson, S. J.: Quantitative Prothrombin and Hippuric Acid Determinations as Sensitive Reflections of Liver Damage in Human Subjects, *J. Lab. & Clin. Med.* 25: 1139, 1940.
41. Kark, R., White, F. W., Souter, A. W., and Deutsch, E.: Blood Prothrombin Levels and Hippuric Acid Excretion Liver Function Test in Liver Disease, *Proc. Soc. Exper. Biol. & Med.* 46: 424, 1941.
42. DeLor, C. J., and Reinhart, H. L.: An Analysis of the Hippuric Acid, Galactose Tolerance, Bromsulphaleum and Prothrombin Tests in 381 Cases, *Am. J. Clin. Path.* 10: 617, 1940.
43. Andrus, W. DeW., and Lord, J. W., Jr.: Unpublished data.
44. Lord, J. W., Jr., Andrus, W. DeW., and Moore, R. A.: Metabolism of Vitamin K and Role of the Liver in the Production of Prothrombin in Animals, *Arch. Surg.* 41: 585, 1940.
45. Stewart, J. D., Rourke, G. M., and Allen, A. W.: Control of Post-operative Bleeding in Obstructive Jaundice, *Ann. Surg.* 110: 693, 1939.
46. Lord, J. W., Jr., and Andrus, W. DeW.: Changes in the Liver Associated With Hyperthyroidism, *Arch. Surg.* 42: 643, 1941.
47. Lord, J. W., Jr.: The Effect of Trauma to the Liver on the Plasma Prothrombin, *Surgery* 6: 896, 1939.
48. Cullen, S. C., Ziffren, S. E., Gibson, R. B., and Smith, H. P.: Anesthesia and Liver Injury, With Special Reference to Plasma Prothrombin Levels, *J. A. M. A.* 115: 991, 1940.
49. Allen, J. G., and Livingstone, H. M.: Studies on Early Post-operative Reduction of Prothrombin in Jaundiced and Biliary Fistula Patient, With Special Reference to Anesthesia, *Anesthesiology* 1: 89, 1940.
50. Smith, H. P., Ziffren, S. E., Owen, C. A., and Hoffman, G. R.: Clinical and Experimental Studies on Vitamin K, *J. A. M. A.* 113: 380, 1939.
51. Dam, H., and Glavind, J.: Vitamin K in Human Pathology, *Lancet* 1: 720, 1938.

52. Rhoads, J. E.: Relation of Vitamin K to the Hemorrhagic Tendency in Obstructive Jaundice, With a Report on Cerophyl as a Source of Vitamin K, *SURGERY* 5: 794, 1939.
53. Illingworth, C. F. W.: Hemorrhage in Jaundice, *Lancet* 1: 1031, 1939.
54. Allen, J. G., and Julian, O. C.: Chemical Use of Synthetic Substance Resembling Vitamin K (2-Methyl-1, 4 Naphthoquinone), *Arch. Surg.* 40: 912, 1940.
55. Hawkins, W. B., and Whipple, G. H.: Bile Fistulas and Related Abnormalities: Bleeding, Osteoporosis, Cholelithiasis and Duodenal Ulcers, *J. Exper. Med.* 62: 599, 1935.
56. Hawkins, W. B., and Brinkhous, K. M.: Prothrombin Deficiency, the Cause of Bleeding in Bile Fistula Dogs, *J. Exper. Med.* 63: 795, 1936.
57. Smith, R. P., Warner, E. D., Brinkhous, K. M., and Seegers, W. H.: Bleeding Tendency and Prothrombin Deficiency in Biliary Fistula Dogs: Effect of Feeding Bile and Vitamin K, *J. Exper. Med.* 67: 911, 1938.
58. Zuckerman, I. C., Kogut, B., Jacobi, M., and Cohen, J. Y.: Studies in Human Biliary Physiology, III. The Effect of Bile and Vitamin K on Experimentally Produced Hemorrhagic Diathesis in the Human With a Total External Biliary Fistula, *Am. J. Digest. Dis.* 6: 332, 1939.
59. Scanlon, G. H., Brinkhous, K. M., Warner, E. D., Smith, R. P., and Flynn, J. L.: Plasma Prothrombin and the Bleeding Tendency With Special Reference to Jaundiced Patients and Vitamin K Therapy, *J. A. M. A.* 112: 1898, 1939.
60. Pohle, T. J., and Stewart, J. K.: Study of the Quick Method for the Quantitative Determination of Prothrombin with Suggested Modifications, *Am. J. M. Sc.* 198: 622, 1939.
61. Stewart, J. D.: Oral and Parenteral Use of Synthetic Vitamin K Active Substances in Hypoprothrombinemia, *SURGERY* 9: 212, 1941.
- 62a. Lord, J. W., Jr., and Andrus, W. DeW.: Differentiation of Intrahepatic and Extrahepatic Jaundice, Response of the Plasma Prothrombin to Intramuscular Injection of Menadiolone (2 Methyl-1, 4 Naphthoquinone) as a Diagnostic Aid, *Arch. Int. Med.* 68: 199, 1941.
- 62b. Andrus, W. DeW., Lord, J. W., Jr., and Lake, M.: Tests of Hepatic and Pancreatic Function in the Differential Diagnosis and Preparation of Patients With Lesions of the Biliary Tract, *Ann. Surg.* In Press.
63. Olm, J. H.: Differentiation of Surgical Jaundice From Severe Damage of the Liver (Subacute Yellow Atrophy) Clinically Simulating It, *Arch. Surg.* 43: 633, 1941.
64. Kark, R., and Lozner, E. L.: Nutritional Deficiency of Vitamin K in Man, *Lancet* 2: 1162, 1939.
65. Scarborough, H.: Nutritional Deficiency of Vitamin K in Man, *Lancet* 1: 1080, 1940.
66. Clark, R. L., Dixon, C. F., Butt, H. R., and Snell, A. M.: Deficiency of Prothrombin Associated With Various Intestinal Disorders. Its Treatment With the Antihemorrhagic Vitamin (Vitamin K), *Proc. Staff Meet., Mayo Clin* 14: 407, 1939.
67. Mackie, T. T.: Vitamin K Deficiency in the Absence of Jaundice, *New York State J. Med.* 40: 987, 1940.
68. Brinkhous, K. M., Smith, R. P., and Warner, E. D.: Plasma Prothrombin Level in Normal Infancy and in Hemorrhagic Disease of the Newborn, *Am. J. M. Sc.* 193: 475, 1937.
69. Hellman, L. M., and Shettles, L. B.: Factors Influencing Plasma Prothrombin in the Newborn Infant I Prematurity and Vitamin K, *Bull. Johns Hopkins Hosp.* 65: 178, 1939.
70. Javert, C. T., and Moore, R. A.: Prothrombin Concentration in Parturient Women and Their Newborn Infants, *Am. J. Obst. & Gynec.* 40: 1022, 1940.
71. Quick, A. J., and Grossman, A. M.: Concentration of Prothrombin in Blood of Babies (1 to 7 Days Old), *Proc. Soc. Exper. Biol. & Med.* 40: 647, 1939.
72. Quick, A. J., and Grossman, A. M.: Prothrombin Concentration in Newborn, *Proc. Soc. Exper. Biol. & Med.* 41: 227, 1939.
73. Norris, R. F., and Rush, A.: Comparison of Prothrombin Levels of Maternal and Cord Blood at Delivery, *Surg. Gynec. & Obst.* 70: 1006, 1940.
74. Kato, K., and Poncher, H. G.: Prothrombin in Blood of Newborn Mature and Immature Infants as Determined by Microprothrombin Test, *J. A. M. A.* 114: 749, 1940.

75. Waddell, W. W., Guerry, D., Bray, W. E., and Kelley, O. R.: Possible Effects of Vitamin K on Prothrombin and Clotting Time in Newly-Born Infants, *Proc. Soc. Exper. Biol. & Med.* 40: 432, 1939.
76. Shettles, L. B., Delfs, E., and Hellman, L. M.: P. . . . Plasma Prothrombin in the Newborn. II. Antepartum Vitamin K Concentration, *Bull. Johns Hopkins Hosp.* 65: 419, 1939.
77. Waddell, W. W., and Guerry, D.: Effect of Vitamin K on the Clotting Time of the Prothrombin and the Blood With Special Reference to Unnatural Bleeding of the Newly Born, *J. A. M. A.* 112: 2259, 1939.
78. Nygaard, K. K.: Prophylactic and Curative Effect of Vitamin K in Hemorrhagic Disease of Newborn (Hypoprothrombinemia Hemorrhagica Neonatorum), Preliminary Report, *Acta obst. et gynec. Scandinav.* 19: 361, 1939.
79. Munimence, A. E., Hellman, L. M., and Shettles, L. B.: Factors Influencing Plasma Prothrombin in the Newborn Infant. IV. The Effect of Antenatal Administration of Vitamin K on the Incidence of Retinal Hemorrhage in the Newborn, *Bull. Johns Hopkins Hosp.* 68: 158, 1941.
80. Tocantins, L. M.: Probable Mechanism of "Physiologic" Hypoprothrombinemia of Newborn, *Am. J. Dis. Child.* 59: 1054, 1940.
81. Andrus, W. DeW., and Lord, J. W., Jr.: Unpublished data.
82. Glynn, M. J.: Bleeding Due to Prothrombin Deficiency During Gastrointestinal Intoxication, *Am. J. Dis. Child.* 62: 1113, 1941.
83. Weller, C. V.: Hepatic Pathology in Exophthalmic Goiter, *Ann. Int. Med.* 7: 543, 1933.
84. Beaver, D. C., and Pemberton, J. deJ.: Pathological Anatomy of Liver in Exophthalmic Goiter, *Ann. Int. Med.* 7: 687, 1933.
85. Shaffer, J. M.: Disease of the Liver in Hyperthyroidism, *Arch. Path.* 29: 20, 1940.
86. Boyce, F. F., and McPetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test: II. Thyroid Disease, *Arch. Surg.* 37: 427, 1938.
87. Bartels, E. C., and Perkin, H. J.: Liver Function in Hyperthyroidism as Determined by the Hippuric Acid Test, *New England J. Med.* 216: 1051, 1937.
88. Crile, G., Jr.: Liver Failure as Factor in Postoperative Delirium in Patients With Hyperthyroidism, *West. J. Surg.* 48: 438, 1940.
89. Shay, H., and Schloss, E.: Painless Jaundice: Its Differential Diagnosis by Galactose Tolerance Test, *J. A. M. A.* 98: 1433, 1932.
90. Schiff, L., and Senior, F. A.: A Study of One Hundred Cases of Jaundice, With Particular Reference to Galactose Tolerance, *J. A. M. A.* 103: 1924, 1934.
91. Banks, B. M., Sprague, P. H., and Snell, A. M.: Clinical Evaluation of Galactose Tolerance Test, *J. A. M. A.* 100: 1087, 1933.
92. Bassett, A. M., Althausen, T. L., and Coltrin, G. C.: A New Galactose Test for Differentiation of Obstructive From Parenchymatous Jaundice, *Am. J. Digest. Dis.* 8: 432, 1941.
93. Hanger, F. M.: Serological Differentiation of Obstructive From Hepatogenous Jaundice by Flocculation of Cephalin Cholesterol Emulsions, *J. Clin. Investigation* 18: 261, 1939.
94. Rosenberg, D. H.: The Cephalin Cholesterol Flocculation Test in Cases of Diseases of the Liver With Special Reference to the Diagnosis of Mild and Unsuspected Forms, *Arch. Surg.* 43: 231, 1941.
95. Pohle, F. J., and Stewart, J. K.: The Cephalin Cholesterol Flocculation Test as an Aid in the Diagnosis of Hepatic Disorders, *J. Clin. Investigation* 20: 241, 1941.
96. Judd, E. S., Snell, A. M., and Hociner, M. T.: Transfusion for Jaundiced Patients, *J. A. M. A.* 105: 1653, 1935.
97. Stewart, J. D.: . . . Deficiency and the Effects of Vitamin K in Obstructive Fistula, *Ann. Surg.* 109: 588, 1939.
98. Lord, J. W., Jr., Andrus, W. DeW., and Moore, R. A.: Quantitative Study of Effect of Transfusion of Blood on Plasma Prothrombin, *Proc. Soc. Exper. Biol. & Med.* 41: 98, 1939.
99. Rhoads, J. E., and Panzer, L. M.: The Prothrombin Time of "Bank Blood," *J. A. M. A.* 112: 309, 1939.
100. Lord, J. W., Jr., and Pastore, J. B.: Plasma Prothrombin Content of Bank Blood, *J. A. M. A.* 113: 2231, 1939.
101. Warner, E. D., DeGowin, E. L., and Seegers, W. H.: Studies on Preserved Human Blood; Decrease in Prothrombin Titer During Storage, *Proc. Soc. Exper. Biol. & Med.* 43: 251, 1940.

102. Ziegler, E. R., Osterberg, A. E., and Hovig, M.: Prothrombin Changes in Banked Blood, *J. A. M. A.* 114: 1341, 1940.
103. Quick, A. J.: The Prothrombin in Preserved Blood, *J. A. M. A.* 114: 1341, 1940.
104. Butt, H. R., Snell, A. M., and Osterberg, A. E.: Phthiocol: Its Therapeutic Effect in the Treatment of Hypoprothrombinemia Associated with Jaundice: A Preliminary Report, *Proc. Staff Meet., Mayo Clinic* 14: 497, 1939.
105. Frank, H. A., Hurwitz, A., and Seligman, A. M.: Treatment of Hypoprothrombinemia With Synthetic Vitamin K; Report of Two Cases, *New England J. Med.* 221: 975, 1939.
106. MacFie, J. M., Bacharach, A. L., and Chance, M. R. A.: Vitamin K Activity of 2-Methyl-1, 4-Naphthoquinone and Its Clinical Use in Obstructive Jaundice, *Brit. M. J.* 2: 1220, 1939.
107. Rhoads, J. E., and Fliegelhuan, M. T.: Use of 2-Methyl-1, 4-Naphthoquinone (Synthetic Vitamin K Substitute) in Treatment of Prothrombin Deficiency in Patients, *J. A. M. A.* 114: 400, 1940.
108. Opie, E. L., and Alford, L. B.: The Influence of Diet on Hepatic Necrosis and Toxicity of Chloroform, *J. A. M. A.* 62: 895, 1914.
109. Johnson, J., Ravdin, I. S., Vars, H. M., and Zintel, H. A.: Effect of Diet on Composition of the Liver in the Presence of Obstruction of the Common Bile Duct, *Arch. Surg.* 40: 1104, 1940.
110. Bollman, J. L., and Mann, F. C.: The Physiology of the Impaired Liver, *Ergebn. d. Physiol.* 38: 445, 1936.
111. Messinger, W. J., and Hawkins, W. B.: Arsphenamine Liver Injury Modified by Diet. Protein and Carbohydrate Protective, But Fat Injurious, *Am. J. M. Sc.* 199: 216, 1940.
112. György, P., and Goldblatt, H.: Hepatic Injury on a Nutritional Basis in Rats, *J. Exper. Med.* 70: 185, 1939.
113. Rich, A. R., and Hamilton, J. D.: Experimental Production of Cirrhosis of the Liver by Means of a Deficient Diet, *Bull. Johns Hopkins Hosp.* 66: 185, 1940.
114. Daft, F. S., Sebrell, W. H., and Lillie, R. D.: Production and Apparent Prevention of a Dietary Liver Cirrhosis in Rats, *Proc. Soc. Exper. Biol. & Med.* 48: 228, 1941.
115. Drill, V. A., and Hays, H. W.: Hyperthyroidism and Liver Function in Relation to B Vitamins, *Proc. Soc. Exper. Biol. & Med.* 43: 450, 1940.
116. Andrus, W. DeW., and Lord, J. W., Jr.: Unpublished data.
117. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, *Bull. Johns Hopkins Hosp.* 47: 338, 1930.

Review of Recent Meetings

SECTION ON SURGERY, GENERAL AND ABDOMINAL, OF THE AMERICAN MEDICAL ASSOCIATION MEETING AT ATLANTIC CITY, N. J., JUNE 8-12, 1942

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THE following papers were presented at the American Medical Association Meeting at Atlantic City, June 8-12, 1942, section on general and abdominal surgery.

Edgar J. Poth, Baltimore: reviewed the experience in the use of succinyl sulfathiazole in the care of patients subjected to large bowel operations. The altered intestinal flora permitted extensive surgical procedures with little danger of local infection or peritonitis, as was shown by a representative series of cases. It was noted that there was a reduction in the incidence of the ordinary complications.

Frank Lahey, Boston: Lesions of the Right Colon Involving Colectomy.—The diagnostic features were presented in 127 resections for lesions involving the right colon. Very advanced cases of secondary anemia can be present in cancer of the rectum and still be operable, while similar lesions in the left colon would indicate inoperability. Lesions involving the terminal ileum of regional ileitis which extend over onto the right colon were presented. The relationship of the infected glands in the entire right mesentery to recurrence of regional ileitis were presented. It was advocated that the right colon, hepatic flexure, and right half of the transverse colon should be removed, in order to remove suspicious mesentery in regional ileitis. In acute stages of regional ileitis, operations should not be performed. The mortality in this series of cases was 11.7 per cent. In the right side of the colon, 53.6 per cent were living at the end of five years.

Harvey B. Stone and Samuel McLanahan, Baltimore: Resection and Immediate Anastomosis for Carcinoma of the Colon.—The method of treatment was presented for resection and immediate anastomosis by the aseptic technique, in which the results obtained were comparable to those achieved by other methods. Statistics were shown in their personal cases, that in the majority of cases such a method could be safely employed. Preliminary or simultaneous decompression of the intestine had been occasionally employed.

Thomas E. Jones, Cleveland: Complications of Combined Abdomino-perineal Operations Presented in 500 Cases.—The most common complication was referable to the bladder, and is probably due to destruction of the sympathetic nerves necessitated by this radical procedure. Infection was shown to cause considerable annoyance. Pulmonary complications were reported to be rare. Wound infections, which formerly occurred in 25 per cent of the cases, had been reduced in the past five years to approximately 2 per cent. Femoral phlebitis and hemorrhage were rare. Prophylactic and therapeutic effort was advocated in the prevention of these complications.

Charles B. Puestow, Chicago: *Experimental and Clinical Studies of Intestinal Motility and Postoperative Distention*—It was noted in experimental evidence that there was a contrary action of the large and small bowels. That is, when one is motile, the other is quiet, and vice versa. Drugs which stimulate small bowel motility, as opiates, prostigmine, physostigmine, and acetylcholine derivatives, inhibit the colon. Drugs which stimulate the colon, as solution of posterior pituitary and pitressin, inhibit the small bowel. The importance of these factors was stressed in the production of gas pains and postoperative distention.

I. S. Ravdin, Philadelphia: *The Prevention of Liver Damage and the Facilitation of Repair in the Liver by Diet*—It was shown that glycogen does not directly protect the liver from injury, and its effect is completely indirect. An adequate amount of proteins in the diet will protect the liver from injury. This action is brought about by the lipotropic action and some direct protection by certain components of the protein molecule. Experimental evidence, both in animals and man, showed what was accomplished by intravenous administration of dextrose and diet. This data was in agreement in that it is not possible greatly to influence the composition of the liver solely by intravenous therapy. A sufficient amount of adequate foodstuffs are necessary to meet the energy requirements of the patient and to provide for deposition in the liver.

J. Ross Veal, Washington, D. C.: *Prevention of Pulmonary Complications Following Thigh Amputations by High Ligation of the Femoral Vein*—Pulmonary complications following thigh amputations were reported as being the chief factor in the high mortality rate. The author advises preliminary high ligation of the femoral vein before amputation to close the source of emboli. In 114 thigh amputations without ligation of the femoral vein, there were 69 deaths, 42.2 per cent of them resulting from pulmonary complications. In 80 thigh amputations in a similar group of vascular gangrene cases in which a preliminary high ligation of the femoral vein was performed, there were 14 deaths. There was only one pulmonary complication. The technique of high ligation of the femoral vein was reported.

W. J. Potts, Oak Park, Illinois: *Pulmonary Embolism*—In experimental work done on dogs, the external jugular and femoral veins were partially occluded with a single silk ligature. No thrombosis followed. In a second group of experiments, the veins were doubly partially occluded with silk ligatures placed 1 to 2 cm. apart. In the external jugular veins, thrombosis developed in one of fourteen experiments. In the femoral vein, thrombosis occurred in twelve of twenty-two experiments. It appeared that an alteration in the rate of venous blood flow was a factor in the formation of thrombi.

Arthur W. Allen, Boston: *Subtotal Gastrectomy for Stenosing Duodenal Ulcer, (Chairman's Address)*—A review of this subject was presented with an analysis of the various factors involved in cure from methods other than subtotal resection of the stomach. It was shown that the results obtained from subtotal gastrectomy were by far more beneficial than by other methods. A motion picture was shown demonstrating the author's method of performing a subtotal gastrectomy. In this procedure, resection is performed from the fundus end and the removal of the pyloric end is done after mobilization of the stomach and first portion of the duodenum.

Harry E. Mock and Harry E. Mock, Jr., Chicago: *Management of Skull Fractures and Brain Injuries*—A study of 462 cases of consecutive proved skull fractures was presented for the purpose of evaluating the best types of management of

brain injuries. These were collected from representative hospitals in every part of the country. The mortality rates varied from 17 to 49 per cent. Over 50 per cent of the hospitals had a mortality rate above 33 per cent. The immediate management of cerebral shock, overcoming anoxemia and ischemia of the injured brain by use of oxygen, adequate dehydration, and spinal drainage, avoiding oversedation, operating when indicated but not too early, and the diagnosis of associated injuries was advised in an effort to reduce the mortality rates.

J. D. Martin, Jr. and Robert Mabon, Atlanta: Pulsating Exophthalmos.—The pathologic aspects of this condition were shown to be well established in the traumatic type, to be a communication between the internal carotid artery or its branches, and the cavernous sinus. Anatomic dissections were presented which established the relationship of these structures, and explained the possibility for the development, both in the traumatic and spontaneous lesions. A review of the literature with the results obtained by the various methods of treatment was presented. It was shown that in ligation of the internal or common carotid artery, the results were essentially the same. A report was made of five cases which were treated by proximal ligation. Two cases were spontaneous in origin; three were traumatic.

George M. Curtis and James D. King, Columbus, Ohio: Blast Injuries to the Lungs.—The pressure wave of the blast from a bomb explosion was shown to produce serious pulmonary injuries without resultant evidence of injury to the thoracic cage. The lesions are principally due to the impact on the body wall of the pressure component of the blast wave. Lung injury without external evidence of trauma occurs more frequently in peace time than has been previously recognized and reported. The mechanism responsible for the cerebral lesion is the hydraulic pressure on the firmly encased central nervous system, resulting from sudden compression of the thoracic cage with consequent violent back pressure on the venous side. After injury, complete rest is essential; every effort should be made to avoid any additional trauma.

Harold L. Foss, Danville, Pa.: Total Hysterectomy.—A total hysterectomy was said to be the operation of choice in malignant processes involving the fundus of the uterus. A simplification of this procedure has been advised. A facilitation of this has been done by the use of a long-handled knife and a right-angle clamp. The mortality rate of total hysterectomy can be lowered by such a procedure.

U. V. Portmann, Cleveland: Classification of Primary Cases of Cancer of the Breast.—The most important factor governing prognosis and indications for different therapy is thought to be the extent of involvement. This can be determined by recognition of clinical and pathologic manifestations. A classification for primary cases of cancer of the breast was presented on clinical and pathologic information.

Frank E. Adair, New York: The Role of Surgery and Radiation in Cancer of the Breast.—A study of 7,215 cases of cancer of the breast treated at the Memorial Hospital in New York was presented. An evaluation of various methods of treatment, including x-ray, radium, and surgery, was made. The results obtained from these various methods has brought about a tendency among many surgeons to consider simple mastectomy followed by roentgen therapy in lieu of the radical amputation.

Robert Elman, St. Louis: Acute Protein Deficiency in Shock, Burns, Intestinal Obstruction and Peritonitis.—These conditions have in common a serious deficiency in the protein content of the plasma. Acute hypoproteinemia is usually, but not

always, easy to detect because it is often masked by dehydration. Replacement therapy is effective largely with rapid correction of protein deficiency. Plasma transfusions produce such a change, although large volumes are sometimes necessary. Saline and dextrose solutions alone are ineffective and often do harm. The intravenous injection of proteins is a newer way of correcting acute protein deficiency and holds great promise of success.

Elliott C. Cutler and Robert Zollinger, Boston: Acute Cholecystitis.—The authors presented three types of acute cholecystitis: (1) Patients in whom signs and symptoms subsided rapidly when treated with rest, removal of pain, and administration of adequate fluids; (2) patients who continue to show increasingly acute signs in spite of general supportive methods; and (3) patients, who in spite of rest and establishment of fluid and chemical balance, change little. It is felt that operation in this group should be performed after thirty-six to forty-eight hours of observation, after one is certain that the patient is not improving.

F. W. Gaarde, L. E. Priekman, and J. H. Raszkowski, Rochester, Minn.: Is the Asthmatic Patient a Good Surgical Risk?—The most important factor in reduction of mortality rate in asthmatic patients depends on careful selection of patients, observance of preoperative and postoperative precautions, and close cooperation between the medical and surgical staffs caring for these patients. A study of 189 consecutive cases of asthma to have major surgery at the Mayo Clinic disclosed that some form of postoperative pulmonary complication, including severe asthma, developed in twenty-five, or 13 per cent of the cases. Four, or 2.1 per cent of the patients died. Operative procedure on the upper part of the abdomen, which resulted in a lowering of the vital capacity, carries a special hazard for patients with asthma.

Wm. Bates, Philadelphia: Intraspinal Administration of Ammonium Sulfate.—The use of ammonium sulfate intraspinally was presented as a new form of therapy to aid in the control of intractable pain. Clinical application of the pitcher plant, *Sarracenia purpurea*, was carried out over a period of ten years. Identification of the ammonium as the active component of the pitcher plant and the action of the ammonium ion on the nerve impulses was demonstrated, showing the optimal concentration of the ammonium salts. The absence of action on the motor nerves was shown in optimal concentration. Selection of patients was reported in which intractable pain was relieved with ammonium salts intraspinally.

THE TWENTY-FIFTH ANNUAL MEETING OF THE AMERICAN BRONCHESOPHAGOLOGICAL ASSOCIATION

PAUL HOLINGER, M.D., CHICAGO, ILL.

THE twenty fifth annual meeting of the American Broncho-Esophagological Association was held July 8 and 9, 1942, at the Hotel Dennis, Atlantic City, N. J.

W. Likely Simpson, Memphis, Tennessee, presided. In his presidential address, Simpson discussed the technical, medical, and organizational problems in broncho-esophagology at the University of Tennessee School of Medicine. Endoscopic work is divided between the departments of otolaryngology and thoracic surgery. The staff of the former is composed of rotating interns, full time residents, and six attending otolaryngologists who divide the service throughout the year. Clinical material is drawn from cases regularly assigned to the department and from consultations with

brain injuries. These were collected from representative hospitals in every part of the country. The mortality rates varied from 17 to 49 per cent. Over 50 per cent of the hospitals had a mortality rate above 33 per cent. The immediate management of cerebral shock, overcoming anoxemia and ischemia of the injured brain by use of oxygen, adequate dehydration, and spinal drainage, avoiding oversedation, operating when indicated but not too early, and the diagnosis of associated injuries was advised in an effort to reduce the mortality rates.

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Samuel Iglauer, Cincinnati: *A Case of Myoblastoma of the Larynx.*—Iglauer presented a case of this type of tumor of the larynx and summarized the eight cases previously reported in the literature. The neoplasm was a pedunculated tumor with its pedicle between the arytenoid cartilages. The exact diagnosis was made only after the tumor had been removed and examined microscopically.

Fletcher D. Woodward and William W. Waddell, Jr. (by invitation), Charlottesville, Va.: *Bronchoscopy in the Newborn.*—The indication for bronchoscopy in the newborn exists after the usual procedures have failed to either clear the lung or establish a diagnosis. By a series of case reports the authors demonstrate that the procedure may be done with safety and benefit to the patient and, consequently, should be used more frequently. Aspiration of secretions in eleven of seventeen newborn infants, two of them premature, resulted in immediate relief of symptoms. In the remainder of the cases the procedure aided in establishing the diagnosis. In one of the infants, a four pound premature one, the diagnosis of congenital absence of the left bronchus and left lung was corroborated by a lipiodal instillation of 2 c.c. of the oil through the larynx, the oil subsequently being aspirated bronchoscopically.

Kenneth A. Phelps, Minneapolis: *Some Further Observations on Tuberculous Tracheobronchitis.*—Phelps presents his opinions regarding tracheobronchial tuberculosis based on over 200 examinations made at Glen Lake Sanatorium in addition to those presented in previously published works. He stresses the fact that the ultimate prognosis in each case is dependent upon the general tuberculosis outlook of the patient and not upon the local disease of the bronchus. He does not believe that collapse therapy is responsible for the tuberculous bronchitis, but rather that it is a failure of successful pulmonary collapse and a cause of chronicity in pulmonary tuberculosis. In his series the lesion occurred almost exclusively in women, 63 to 2. The sanatorium population was 52 per cent men and 48 per cent women. The most reliable clinical signs of bronchial tuberculosis were found to be those due to an obstruction of the bronchus, namely, a wheeze or retention symptoms, and a positive sputum. Roentgenologically, obstructive emphysema, atelectasis, tennis ball cavities, bronchograms, and laminograms gave evidence of bronchial tuberculosis. Bronchiectasis was proved to exist in 80 per cent of the cases and was suspected in 16 per cent more. Regarding therapy, Phelps states guardedly that local application of 30 per cent silver nitrate helps many patients. Some become sputum free, at least for a while, some breathe better and apparently heal more quickly. In his experience, local treatment of the fibrotic stenoses by dilatation is not satisfactory. End results of his series are 31 per cent dead in five years, 63 per cent have chronic disease, and 6 per cent are well.

Edward A. Looper, Baltimore: *Bronchoscopic Involvement in Purpura Hemorrhagica.*—Looper described the case of a male patient, 31 years of age, who gave a history of repeated attacks of hemoptysis during the past seven months. Tuberculosis, malignancy, and bronchiectasis had been suspected but were not confirmed by the bronchoscopic findings. Numerous blood clots and mucus but no ulcerations of the mucous membrane were seen. The patient died some months later, and the post mortem examination revealed the diagnosis to be purpura hemorrhagica. This case was presented to place it on record as one of the causes of undiagnosed cases of severe pulmonary hemorrhage.

other departments with the exception of the department of chest surgery, which makes its own bronchoscopic examinations. From a clinical standpoint, cases of non-specific esophagitis associated with anemia are found to be of particular interest. Simpson reviewed this subject and added that the clinical picture is still as puzzling as it was twenty five years ago.

F. W. Davison, Danville, Pa., presented a case report of a male, aged 70 years, who for three years had had a sensation of fullness in his throat but had no real dysphagia. When gagged, he regurgitated a long, pink, smooth mass of tissue one inch in diameter, which hung down two inches below his chin. Direct laryngoscopy showed that the pedicle was attached to the left lateral wall of the laryngopharynx. It was ligated and excised with the cutting current. It measured eight inches in length and one inch in maximum diameter, and histologic section showed it to be a fibrolipoma.

Emil Lois Van Loon and Sidney Diamond (by invitation), Philadelphia. **Foreign Bodies in the Gastrointestinal Tract**—They discussed the problem of management of foreign bodies which had reached the stomach or intestines, as illustrated by analysis of the records of 386 consecutive cases of radiopaque foreign bodies in the stomach or intestines seen in the Chevalier Jackson Bronchoscopic Clinic at Temple University Hospital. Thirty eight per cent were in the stomach and 62 per cent in the intestine when first seen. Of the more common foreign bodies, 49 were straight pins, 40 coins, 40 open safety pins, 29 closed safety pins, 29 bobby pins and 26 nails. Most of the patients were small children. Nineteen (48 per cent) of the forty with open safety pins were infants less than one year of age. There was no mortality in this group of 386 patients. In 17 patients in whom the foreign body did not pass beyond the pylorus, it was removed by fluoroscopically guided open tube gastroscopy in 14 and by external operation in 3. Duodenotomy was done in 4 cases. Penetration of the gastric or duodenal wall by the point of the foreign body led to laparotomy in 5 cases. In only one of these cases had perforation been accompanied by symptoms of the perforation, but the diagnosis had been established roentgenologically in each instance.

L. Chester McHenry, Oklahoma City. **Two Cases of Mediastinitis Following Esophageal Foreign Bodies**—Two patients were presented, each of whom had had evidence of cervical mediastinitis upon admission, following attempted swallowing of bones. External surgical drainage was necessary in each case, and, although a very stormy clinical course ensued, both eventually completely recovered. In neither instance was the foreign body recovered. The author stressed the importance of chemotherapy in the management of these patients.

Sydney S. Gellis (by invitation) and L. Emmett Holt, Jr. (by invitation), Baltimore. **The Prophylaxis of Lye Strictures of the Esophagus**—Gellis and Holt describe the technique and results of the Salzer method of the treatment of lye burns of the esophagus as routinely employed at the Harriet Lane Home. Immediate attempts are made to neutralize the corrosive with weak acid, and visible burns are treated locally. Dilatations are started with bougies in the form of soft rubber catheters, 14 to 30 French, tapered and closed, filled with small lead shot. Dilatations are done daily and are begun at once unless there is great swelling of the fauces, when they may be postponed no more than three or four days. The child is held in a sitting posture during dilatation. Dilatations are done daily for two weeks, three times a week for two weeks, twice a week for two months, once a week, three times a month, and two or three times a year for several years. Of 11 children adequately treated according to Salzer's method, only one developed a stricture. Of 14 who received no treatment, 6 developed strictures. Not a single accident and

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In the discussion, **A. H. Andrews, Jr., Chicago**, warned against the use of this method in cases of foreign bodies with the point downward and the head fixed in edematous bronchial mucosa due to the possibility of perforation of the lung by the point with a resultant empyema.

M. C. Myerson, New York City: A Bronchoscopic Diagnostic Sign for Pleural Cavity Lesions.—Myerson has noted varying degrees of passive congestion in circumscribed areas of the bronchial tree during bronchoscopic examinations of patients with lesions in the pleural cavity. This bronchoscopic finding is offered as a new diagnostic sign.

William A. Hudson, Detroit: Carcinoma of the Esophagus; Some Observations With Two Case Reports.—Hudson presented two cases of postcricoid carcinomas of the esophagus which were seen relatively early. In the first a laryngectomy was done and the tumor removed in its entirety. While still further plastic repair is contemplated, the patient is alive, well, and happy three years after the operation and has maintained her weight. In the second case, with a lesion similar to that of the first, the patient refused the extensive surgery recommended and has had a recurrence of her lesion in the larynx itself, the area the patient had refused to allow to be removed. Hudson stresses the importance of the removal of the entire larynx as well as the esophagus when the common partition is involved.

William A. Lell, Philadelphia, Pa.: Bronchoscopy as an Aid in the Treatment of Allergic Pulmonary Disease.—The author pointed out that bronchoscopic aspiration of patients in status asthmaticus is associated with remarkable relief. It aids diagnostically through direct inspection, ruling out lesions such as foreign bodies and tumors which may simulate status asthmaticus. An aid in treatment is the collection of uncontaminated bronchial secretions for bacteriologic study and preparation of an autogenous vaccine. The results of a large series of cases treated bronchoscopically were reviewed and pathologic changes in the lungs, as observed at autopsy in five cases, were presented.

At a combined meeting of the **American Broncho-Esophagological Association** and the **American College of Chest Physicians**, held Monday afternoon, June 8, under the chairmanship of **W. Likely Simpson** and **J. Winthrop Penbody**, presidents respectively of these two organizations, the following papers were presented.

Louis H. Clerf, and C. J. Bucher (by invitation), Philadelphia, Pa.: Adenoma (Mixed Tumor of the Bronchus).—Of a total of 278 cases of primary bronchial

neoplasms that these men have examined, 35, or 12 per cent, have been the benign glandular tumors of the bronchus now called adenomas. Originally these were classified as adenocarcinomas and endotheliomas. Of their 35 patients with adenomas, 13 per cent were less than 20 years of age, 51 per cent of them females. Hemoptysis was an early symptom in 16 per cent, atelectasis in 15 patients, obstructive emphysema in 1, and almost all had had one or more attacks of pneumonia. The tumor was found in the left lung in 24 patients, in the right in 11. The bronchoscopic findings in these cases consist of partial or complete obstruction of the bronchus by a smooth mass. Attention must be noted. However, the authors emphasize the fact that the bronchoscopic appearance of the lesion gives no evidence of what may be present outside of the bronchus. Tomography may aid in obtaining this information. Treatment depends on a number of factors. Bronchoscopic removal of the lesion is advised if this is possible, but surgical removal is indicated if there is evidence of extrabronchial extension of the tumor. Some of the cases reported have been under observation for as long as fifteen years, and one patient is alive and well twelve years after electrocoagulation of the tumor. Of the patients presented in this paper, there have been four deaths which have resulted directly from the tumor. Two of these resulted from bronchiectasis, one from pneumonia which probably was dependent on bronchial obstruction and one from carcinoma which developed at the site of an adenoma of five years' duration. There were four deaths due to unrelated causes. One of these patients had been free from tumor for eleven years. Seven patients are well and free from symptoms although there still is evidence of tumor present. Four patients have tumor with symptoms present; three of these have definite bronchiectasis and a fourth has paroxysms of coughing with occasional infection distal to the tumor which is an extrabronchial producing compression stenosis. This patient undoubtedly has bronchiectasis distal to the stenosis. Two patients have bronchiectasis without symptoms and an absence of tumor. They have been tumor free for seven and ten years respectively; seven are tumor free for periods varying from five to eleven years and also are free of symptoms. One has adenoma in both main bronchi and presents a hopeless problem. Three recently have come under observation. Two of these should be treated surgically for in one the tumor in the right upper lobe bronchus is inaccessible to bronchoscopic treatment and the other has a large extrabronchial tumor in the lower lobe of the left lung which is producing compression stenosis. The third case is being treated bronchoscopically. Prolonged treatment has been recommended in six cases because of inaccessibility of the tumor to bronchoscopic treatment, the presence of extrabronchial adenoma at the occurrence of chronic pulmonary complications which cannot be relieved because of bronchial obstruction. Three have been treated surgically by lobectomy and two by pneumonectomy. There was one operative fatality. This patient had an empyema and was a poor surgical risk.

In the discussion, John Kernan, New York, emphasized the early age of patients in whom the diagnosis of adenoma had been made. Three of his patients were 13, 14, and 17 years old, respectively, and one, a patient of 46 years of age, had had symptoms since 1910. He was of the opinion that all these patients should have surgical removal of the involved lobe or lobes, since he felt the tumors all recurred, or were complicated by bronchiectasis in the lung distal to the tumor. In closing the discussion, G. J. Bucher, Philadelphia, described the microscopic appearance of the lesion, dividing adenomas into three groups: First, those with well-formed alveoli, with few of the cells in mitosis; second, those with a less evident alveolar arrangement with large glands and large cells; third, those containing considerable fibrous tissue, with masses of cells in cylindrical form or in clusters. He stated the tumors are covered with bronchial epithelium but have no capsule. There was no correlation between the histologic classification and the clinical course of the disease in these patients.

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Book Reviews

Roentgen Treatment of Injections By James F. Kelly, M.D., and D. Arnold Dowell, M.D. Cloth. Pp. 132, with 122 illustrations. Chicago, 1942, The Year Book Publishers.

This readable book emanates enthusiasm for the use of roentgen therapy to a degree not supported by most physicians. There are several sections with which general agreement will be found, such as those dealing with treatment of suppurative parotitis and erysipelas, but in regard to gas bacillus infection, peritonitis following appendicitis, and pneumonia, the book is far less convincing. With regard to gas bacillus infection, inadequate controls are given, either in treatment of the developed disease or in prophylaxis. The figures to support the argument for the efficacy of roentgen therapy are drawn from different eras and areas and from different types of accessory treatment and authors, from the so called "control" observations. In the treatment of peritonitis following appendicitis, the figures are also unconvincing, for, although the mortality rates for peritonitis treated with supportive measures and roentgen radiation are very little higher than a recent report on results using conservative measures alone, the control group showed mortality rates so unusually high (65 per cent) that one is led to doubt the value of the comparison. In regard to the treatment of pneumonia, individual cases are presented without control data, and one is at a loss to decide for himself the value of the therapy.

Despite these objections, the volume is very readable, and it provides a reference book of details of treatment which should certainly be borne in mind in the further evaluation of roentgen therapy of infections.

The Management of Fractures, Dislocations, and Sprains By John Albert Key and H. Earle Conwell. Ed. 3. 1303 pages, 1259 illustrations. St. Louis, 1942, C. V. Mosby Company.

All surgeons familiar with the previous editions of this eminently successful text, appearing in 1934 and 1937, will undoubtedly receive the third edition with eagerness and enthusiasm. The book is divided into two parts and arranged in a manner similar to that of the previous editions. However, many of the chapters have been completely revised and rewritten with the inclusion of more modern concepts of therapy and current and timely considerations of certain types of injuries. Thus, the chapter on Compound Fractures includes a new section on war injuries. Moreover, the therapeutic considerations in this chapter have been completely rewritten to conform with the current concepts based upon the use of the sulfonamides. Noteworthy changes have also been made in the chapters on fractures of the humerus, hip, foot, and on injuries of the spine, in which is included a section on lesions of the intervertebral disc and of the ligamentum flavum. In general, the book is an authoritative, comprehensive, and up to date consideration of the subject, and in view of the current conflict, in which such conditions assume greater significance, the book will be received with even more enthusiasm than the previous editions.

Paul H. Holinger, Chicago, Illinois. **Kodachrome Visualization of the Physiology and Pathology of the Tracheobronchial Tree.**—Color motion pictures taken through the bronchoscope were used to demonstrate various physiologic phenomena which occur in the normal bronchial tree. The film presented showed the increase and decrease in the diameter of the bronchi as well as the lengthening and shortening which occurs with respiration. By means of foreign bodies introduced into the bronchi of anesthetized dogs, various obstructive phenomena were illustrated. The mechanism of a wheeze, of the check valve and ball valve obstruction, and of complete obstruction producing atelectasis were shown as they appear bronchoscopically. To illustrate these various phenomena in the human being, the trachea and bronchi of patients with obstructing lesions were photographed bronchoscopically. Bronchiectasis, asthma, pulmonary adenoma, and bronchogenic carcinoma having distinct bronchoscopic features served to demonstrate the physiologic and pathologic processes of the bronchi.

The camera devised for this endoscopic photography consists of a magazine loading 16 mm camera and an f2.7 three inch lens. Illumination of the small endoscopic field is obtained by directing the image of the ribbon of a ribbon filament projection lamp onto a forty five degree mirror which encroaches on the lumen of the endoscope. This type of axial illumination provides adequately the illumination essential to color photography. A specially constructed telescope inserted into this system permits visualization of the field being photographed not only during the finding but also during the actual filming.

Book Reviews

Röntgen Treatment of Infections By James I' Kelly, M.D., and D. Arnold Dowell, M.D. Cloth. Pp. 112, with 122 illustrations. Chicago, 1942, The Year Book Publishers.

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Surgical Physiology. By Joseph Nash, M.D. Ed. 1. Pp. 496. Springfield, Ill., 1942. Charles C Thomas. \$6.00.

This book might well be called a textbook of physiology for surgeons. It deals with physiologic processes of special interest to the surgeon. The practical aspects of pathologic physiology are emphasized, yet rightfully the author expends greater time and space in interpreting normal physiologic processes. As far as this reviewer's experience goes, a text just like it, covering the broad field of physiologic processes in surgery, has never appeared previously. Rost's *Pathological Physiology of Surgical Diseases* had a distinctly more clinical and less physiologic viewpoint than that reflected in this book. It is evident that the author of this monograph has a valuable background of training in the teaching of physiology. Now that he has identified himself with clinical surgery, it is to be hoped that in successive editions he will be enabled to bridge even more usefully the rather broad gap still existing between the discovery of physiologic fact and its adoption in practice in the clinic.

This is a useful and important book. It can be recommended enthusiastically to surgeons. A careful perusal of it will help surgeons to a better understanding and interpretation of normal and disturbed physiologic processes and thereby make them better surgeons.

Diseases and Injuries of the Larynx. By Chevalier Jackson, and Chevalier L. Jackson. Cloth. Pp. 663, with 200 illustrations. Philadelphia, 1942, W. B. Saunders Company. \$8.

When Jackson and Jackson, in 1937, published their first edition, it received a warm welcome and was readily acclaimed the best book on this subject in the English language.

The authors now have published their second edition which incorporates much of the first plus the added developments in the field of laryngology up to the present time.

Every phase of laryngology is discussed in that typical and thorough style which so characterizes the Jacksons. Therapy and surgery for all conditions pertaining to the larynx are discussed at length and the new King operation for bilateral recurrent paralysis is given due recognition.

Probably one of the most interesting chapters in this book is the one on war surgery of the larynx which discusses all laryngeal trauma of war as well as of industrial and accidental surgery. This particular chapter should be read by every laryngologist.

This work is an outstanding contribution to laryngology by men whose clinical experience and scientific research eminently qualify them to produce such a masterpiece.

Carcinoma and Other Malignant Lesions of the Stomach. By Waltman Walters, B.S., M.D., M.S., Howard K. Gray, B.S., M.D., M.S., and James T. Priestly, B.S., M.D., M.S., Mayo Clinic and Mayo Foundation, Rochester, Minn. Ed. 1. Pp. 576, with 141 illustrations. Philadelphia, 1942. W. B. Saunders Company.

This monograph summarizes the experience of the Mayo Clinic with the management of carcinoma of the stomach over a forty year interval (1907 to 1938). During that period of time 6,242 patients with cancer of the stomach were submitted to operation. Resection was done in 2,772 or 44.4 per cent of the patients operated upon. The mortality of the resection group was 16.2 per cent, a remarkable achievement considering the years of treatment under discussion. This is an

accomplishment, for the period, which excels the best performance of American surgical clinics in dealing with cancer of the stomach, speaking eloquently for the high standard of the surgery established by the Mayo brothers. At the present time, it should be remarked that this record of accomplishment is being equaled and surpassed today in many surgical clinics in America, affording proof that surgery is being improved, not alone by progress within the specialty itself, but also through new discoveries in related fields.

Perhaps the most valuable portions of this monograph are the detailed tables in the last section of the book, detailing the various factors which bear on operability, mortality, and prognosis. Whereas only 62 per cent of patients observed to have carcinoma of the stomach survived five years, the writers found that 28.6 per cent of the resection group survived for five years; at ten years, 20.3 per cent were still alive; at fifteen years, 15.5 per cent, and at twenty years after resection there were 10.4 per cent surviving. This table (page 515) gives adequate proof of the curability of favorable types of cancer of the stomach.

The authors have a number of collaborators who help to complete the surgical picture of the disease, emphasizing the current practices and teachings of the Mayo Clinic group with reference to carcinoma of the stomach. Especially valuable chapters are contributed by Snell, Broders, MacCarthy, and Berkson.

The statistical analysis of this material from one clinic constitutes an important contribution to the surgical literature of carcinoma of the stomach.

Skin Grafting. By E. C. Padgett. 149 pp, 87 illustrations. Springfield, Ill., 1942. Charles C Thomas, Publisher. \$4.50.

This small monograph by Dr. Padgett is a very welcome and admirable addition to the literature of the subject of transplantation of skin. In eleven well chosen chapters, the author traces briefly the historical aspects of skin grafting, the important item of homotransplantation, and the histology of grafts, as well as the various types of skin grafts and the problems incidental to the various sites to be grafted and types of grafts employed.

The author's own very important contribution to skin grafting, the dermatome and its use, is well described. Unquestionably, this is one of the best books that has ever been written on the subject of skin grafting. It is recommended enthusiastically to all who concern themselves with this interesting and important phase of surgery.

Diseases of the Thyroid Gland. By Arthur E. Hertzler. 670 pages, with 354 illustrations. New York, 1941, Paul B. Hoeber, Inc. \$8.50.

As the author states, this book is a record of his studies of diseases of the thyroid extending over a period of nearly fifty years. There are few doctors who have studied their cases as carefully from the point of diagnosis, pathology, and treatment. One may not agree with the author's ideas concerning the histology of the various diseases of the thyroid gland nor his recommendations for total thyroidectomy; however, for the most part, his ideas of treatment are more or less along the generally accepted lines and the book is an acceptable review of diseases of the thyroid.

There are some objections that might be voiced against a medical book of this type. While "slapstick" humor may be part of one's personality, too much of it in a medical book is not only tiresome but also detracts from the dignity of the volume. Also, in writing a book on a medical subject, one should express himself chiefly as an authority of the medical subject at hand rather than a prophet in matters of religion, politics, or social conduct. When the author makes such

statements as "I have done many thyroidectomies without any sterile sheets", "the face mask has for its chief purpose to cover the operator's embarrassment at his ignorance of anatomy," one is tempted to remind the author that before the days of aseptic surgery patients often recovered from operations.

The printing and illustrations are excellent; the only flaw in the printing occurs on page 515 in the discussion of "toxic crisis." A workable index is appended.

Wounds and Fractures. A Clinical Guide to Civil and Military Practice. By H. Winnett Orr, M.D., F.A.C.S., Nebraska Orthopedic Hospital. Pp. 227, illustrations 137. Springfield, Ill., 1941, Charles C. Thomas, Publisher. \$5.00.

In this monograph the author sets forth his ideas concerning the treatment of wounds of the extremities. His method of management of compound injuries of the extremities has become well known and is practiced widely. The text is essentially a digest of the author's own experience. It is in no sense a comprehensive treatise on wound management. Even in the author's own province, the work of V. Bergmann (1874) and F. E. Dennis (1884), the American surgeon, is not mentioned. The latter author treated compound fractures by immobilization in plaster as long ago as 1884, and was then able to record 154 cases without a death from septic infection and 100 cases without a death from any cause. Quite a remarkable achievement. The author gives no attention to the important item of physical factors concerned in the management of infection. Further, there is no account of the use of the sulfonamides in the treatment of infections of the extremities, a rather serious omission.

Nevertheless, this text affords the general surgeon and the orthopedist an opportunity to become familiar with the latest comprehensive expression from H. W. Orr on wound management. A useful reference list of his own writings on the subject is appended. The Orr method, in the hands of those familiar with its use, has saved many lives and constitutes an important agency in wound management. The book can be recommended as constituting an excellent summary of Orr's teachings and practice.

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Original Communications

LIGATION OF THE PATENT DUCTUS ARTERIOSUS

A REPORT OF THE RESULTS IN SEVEN CASES

GEORGE H. HUMPHREYS, M.D., NEW YORK, N. Y.

(From the Department of Surgery, Babies Hospital, and of the College of Physicians and Surgeons, Columbia University)

THE possibility of successfully obliterating by surgery a ductus arteriosus which has remained patent beyond the neonatal period was established over two years ago by Gross and Hubbard. The number of reported cases in which the procedure has been carried out is, however, still small. As a result the risks of the procedure as well as its late results are still a matter of some uncertainty, and the indications for attempting it are not yet generally agreed upon. Since clarification of these points can come only through accumulation of experience, it seems worth while to present case reports, to review the reasons for operating, and the results obtained.

All of these patients were children between 9 and 13 years of age. They were selected from a group of twenty children in which the diagnosis of patent ductus arteriosus without other cardiovascular anomaly had been made, which had been referred for consideration of surgery. All were thought to show evidence that the continued patency of the ductus was resulting in deleterious effects, and two had evidence of complicating subacute blood stream infection. The first patient was not only poorly developed and nourished, but had had evidence of diminished cardiac reserve for several years, with one episode of mild congestive failure. The second patient also showed diminished cardiac reserve but without failure, and in addition had a long record of recurrent respiratory infection, with poor appetite and nutrition though normal development. The third patient had a similar record of repeated respiratory infection, poor appetite and nutrition, but normal development and little or no diminution of cardiac reserve. The fourth and fifth patients

Received for publication, May 1, 1942

statements as "I have done many thyroidectomies without any sterile sheets", "the face mask has for its chief purpose to cover the operator's embarrassment at his ignorance of anatomy," one is tempted to remind the author that before the days of aseptic surgery patients often recovered from operations.

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Beginning in 1934, at about the age of 6, she began to find it difficult to keep up with other children at play. She had occasional epistaxes and noticed increasing dyspnea and precordial discomfort associated with palpitation on exertion. Because of these symptoms during the three years prior to admission she had been followed in the cardiac clinic of the Greenpoint Hospital, and had been put in a special cardiac class at school.

In March, 1939, she first noticed ankle edema, with tenderness on pressure on the left. She was admitted to Greenpoint Hospital and while there an abscess formed at the tip of her left great toe. This broke spontaneously, discharged pus for a short time, then healed. She was transferred on May 25, 1939, to Kings County Hospital. Physical examination at this time showed marked malnutrition, underdevelopment, and a chest deformity of pigeon breast type, without other evidence of rickets. There was a continuous precordial thrill and loud continuous murmur with systolic accentuation. Her arterial blood pressure was 96/38 and her venous pressure 170. The liver could be felt one and one-half fingers below the costal margin. X-ray of her chest showed an enlarged left auricle and ventricle and accentuated conus.

On June 21, 1939, she was discharged for convalescence to Seaside Hospital, with a diagnosis of patent ductus arteriosus. She remained there, in bed, until Aug. 27, 1939. During this time she ran an intermittent low-grade fever and showed a constantly elevated sedimentation rate (about 30 mm. per hour). Wassermann was negative; Mantoux, positive. Urine and blood counts were not remarkable. The foot showed variable swelling and tenderness but never redness, heat, or purulent discharge. Other findings confirmed those noted at Kings County Hospital. She was discharged, Aug. 28, 1939.

The patient was admitted to Babies Hospital on Sept. 11, 1939, for ligation of the patent ductus. Examination showed: Temperature 100°; sedimentation rate, 49 mm. per hour; white blood count, 20,950; urine, negative; Mantoux, negative 0.01 Gm., positive 0.1 Gm.; blood pressure, 95/45 (right arm); venous pressure, 95. She was a poorly developed girl, showing pronounced malnutrition, adenoid facies, and a narrow chest with pigeon breast deformity of the sternum. Her feet were flat and of peculiar shape; there was a scar on the terminal phalanx of the left great toe and the left ankle was slightly edematous. Her heart was slightly enlarged with an almost continuous thrill over the whole precordium, most pronounced over the third left interspace. Sounds over the right base were of fair quality, elsewhere they were obliterated by a loud "machinery" murmur with systolic accentuation. The systolic murmur was transmitted to neck and back. No cyanosis or clubbing were present.

X-rays of chest showed prominence of pulmonary conus and accentuated bronchovascular markings. Kymography and fluoroscopy showed pulsations of hilar shadows. X-rays of feet showed bilateral congenital anomalies of the third metatarsals. The right astragalus showed deformity and periosteal reaction of obscure etiology. Electrocardiogram showed no significant alteration from normal.

Operation was done Oct. 3, 1939. A ductus about 1 cm. in diameter and 0.8 cm. long was doubly ligated according to the technique described by Gross. Endotracheal ether anesthesia was used.

Postoperatively her immediate response was excellent. Twenty-four hours after operation she developed marked dyspnea due to laryngeal and tracheal edema associated with profuse mucoid discharge. X-rays showed some density at left base, probably atelectasis. These symptoms subsided during the next three days. Her temperature varied up to 102° for the first four days, was normal after the fifth. The wound healed by primary union, stitches being removed on the sixth day. She was up on the seventh day, home on the twelfth. On discharge her heart showed

both showed marked retardation of growth and development though their nutrition and cardiac reserve were not conspicuously affected. The fifth patient developed a subacute blood stream infection and a recurrence of patency of the ductus, for which a second operation was performed. The sixth patient showed poor nutrition, delayed growth and development, and frequent respiratory infections, but little diminution of cardiac reserve. Subacute blood stream infection was the primary indication for operation on the seventh patient, who otherwise showed poor nutrition but little delay in growth and no appreciable diminution of cardiac reserve. The factors which influenced the decision to operate are summarized in Table I.

The physical signs and data obtained from x-ray, electrocardiographic and electrostethographic studies, on which the diagnosis in each case was based, are described in the individual case histories. It is interesting to note that in several cases, one or more of the usual diagnostic criteria were absent, yet in every child explored a patent ductus was found. A low diastolic pressure was the most consistent finding. Studies of pulmonary ventilation and cardiac output were also made in several of these patients and will be reported in a separate paper. Associated skeletal anomalies were present in three children, and a congenital squint and torticollis were present in another.

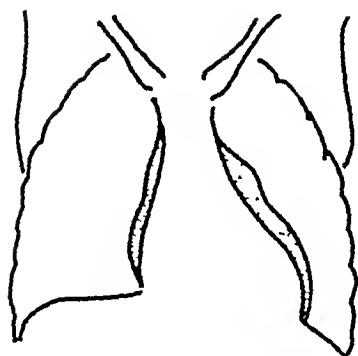
TABLE I
SUMMARY OF FACTORS INFLUENCING DECISION TO OPERATE

PATIENT	CARDIAC FAILURE	DIMINISHED CARDIAC RESERVE	CHRONIC MALNUTRITION	DELAYED GROWTH AND DEVELOPMENT	REPEATED RESPIRATORY INFECTIONS	SUBACUTE BLOOD STREAM INFECTION
R.R.	+++	++++	++++	+	±	0
R.B.	±	+++	+++	0	++++	0
F.F.	±	+	++	±	++++	0
J.B.	0	0	++	++++	±	0
T.Y. a.	0	0	+	++++	±	0
R.H.	0	0	+++	+++	+++	0
T.Y. b.	0	0	+++	++++	±	<i>Staph. aureus</i>
J.M.	0	±	+++	±	++	<i>Str. viridans</i>

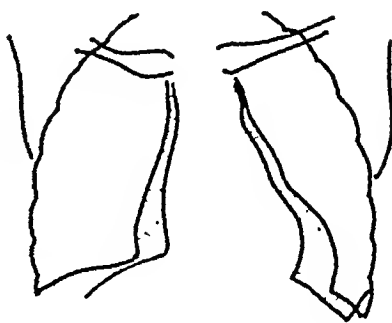
CASE REPORTS

CASE 1.—R. R. was born at home on March 22, 1928, a normal full-term delivery. She was the sixth of eight children of an Italian laborer, whose wife is also his first cousin. Both parents are in good health. The third child, aged 18 years, is an imbecile; the seventh child, aged 8 years, has celiac disease; the eighth child died at three months of unknown cause; the other four children are well and normal as far as known. There is no known history of tuberculosis or heart disease in the family, but the parents are vague as to the health of relatives in Italy.

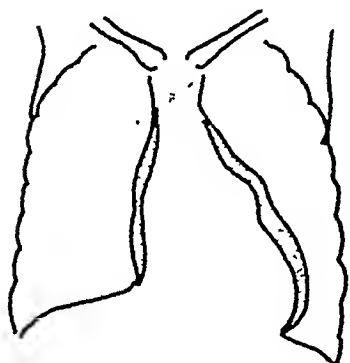
Her neonatal period was uncomplicated. Shortly after her birth her mother was told that the baby had heart trouble for which nothing could be done. In spite of this her early childhood development was not retarded; she had no blue spells, no cardiac symptoms, and was able to keep up in school. She went through measles, and chicken pox without sequelae, and had no joint pains or chronic fever. Until the present illness she had had no injuries or operations.



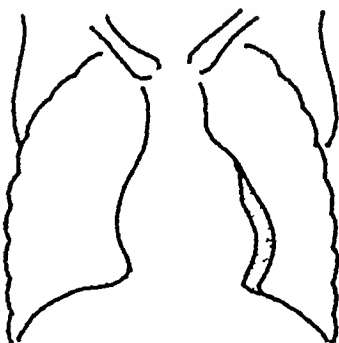
Case 1.



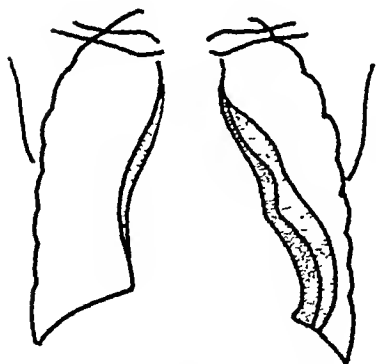
Case 2.



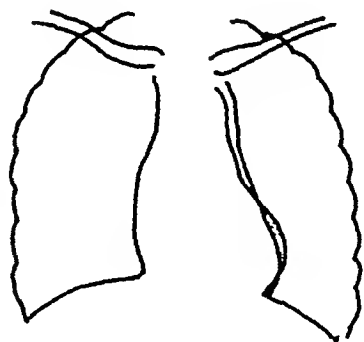
Case 3.



Case 4



Case 5.



Case 7.

Fig 2—Tracings of roentgenograms to show changes in the size and shape of the cardiac shadow following ligations in six patients. The most striking change is a decrease in the left ventricular shadow. The "pulmonary conus" shadow disappeared in Case 1, and decreased in size in Cases 2 and 5, but in Case 3 it became more conspicuous and in Case 4 it appeared only after ligation. Case 7 showed none of the changes associated with a patent ductus, and changed very little following ligation.

complete absence of the previous thrill and murmur. X-rays showed disappearance of the pulmonary conus bulge, no pneumothorax, slight density at left base suggesting residual atelectasis, and bronchovascular markings less dense. X-rays of feet showed a new lesion involving the first left metatarsal. She was discharged, walking, Oct. 15, 1939.

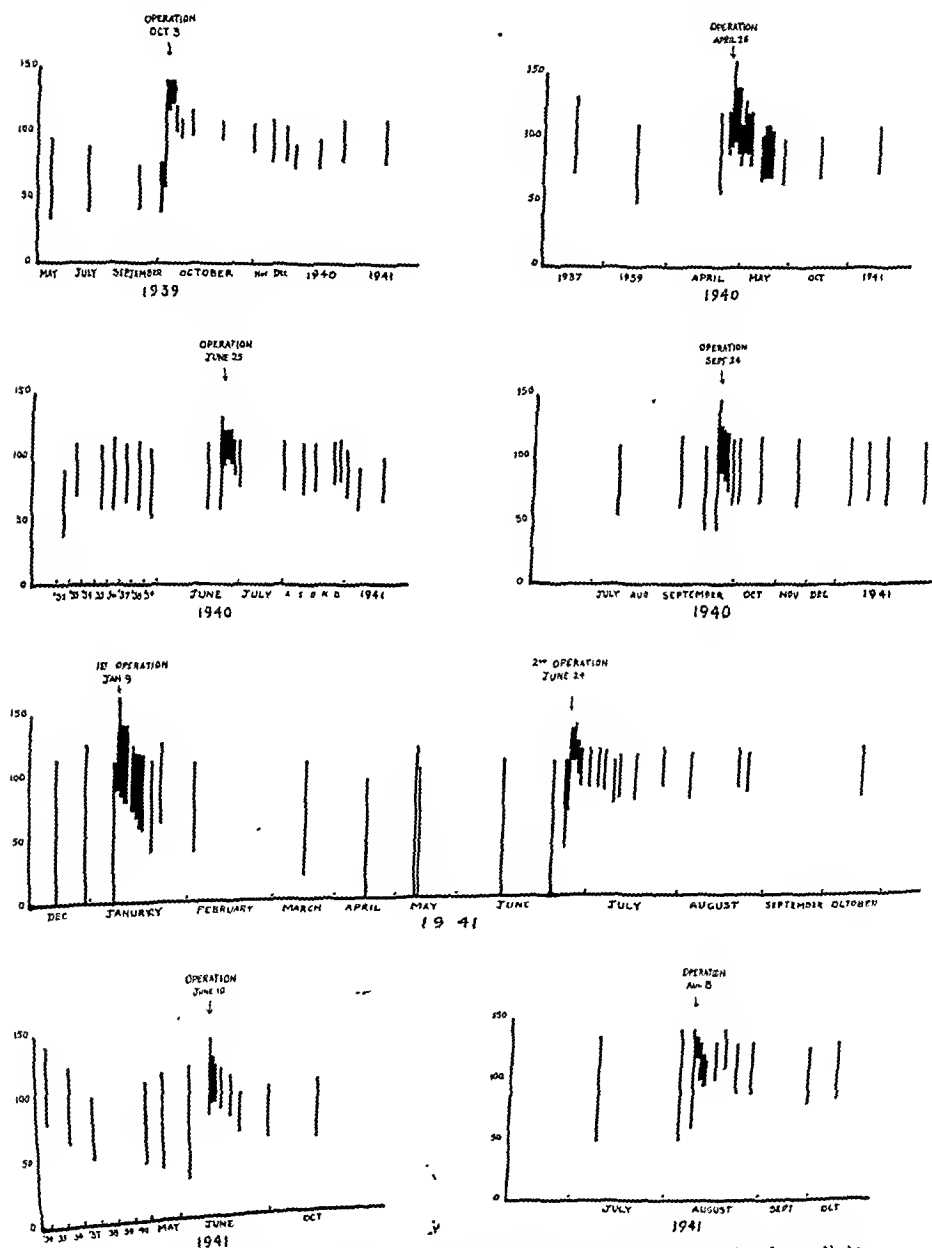


Fig. 1.—A chart of blood pressure readings before operation, in the immediate postoperative period, and in the follow-up period showing the response to eight ligations in seven patients. In every instance both systolic and diastolic pressures rise abruptly following ligation, then fall during the postoperative period to a new level, with pulse pressure lower and diastolic pressure higher than before operation.

dyspnea, orthopnea and generalized lymphadenopathy. His heart was enlarged outward and downward and showed marked tachycardia, gallop rhythm, a thrill over the entire precordium, and a machinery-like murmur at the base. At this time the joint pains, together with an x-ray cardiac shadow which was not considered typical of patent ductus, and the fact that both systolic and diastolic murmurs could be heard at the apex raised the question of a possible superimposed rheumatic heart disease. However, laboratory evidence failed to substantiate this. He improved rapidly on bed rest and after being allowed up a week after admission it was found that arch supports relieved his leg pains.

During the next two years his cardiac function remained much diminished, so that he could not climb stairs without marked dyspnea and was able to play no active games. He attended a cardiac class in school and efforts to maintain nutrition and general resistance were unremitting. In spite of this, though he grew and developed normally for his age, his weight became increasingly below average for his height and age.

He was admitted to Bellevue Hospital on Dec. 26, 1939, for ligation of the patent ductus. Examination showed: Temperature, 99°; pulse, 100; respirations, 22; blood pressure, 110/50; height, 5 feet 4 inches; weight, 87 pounds. He was a swarthy boy, underweight but not undersize for his age, who showed some persistent mucopurulent postnasal discharge. There was no cyanosis, clubbing of fingers, edema, or other abnormality of abdomen or extremities. His heart showed diffuse enlargement with the maximum impulse in the anterior axillary line in the fifth intercostal space, forceful and much more prominent than normal. A systolic thrill was present at the second left intercostal space where a loud machinery-like murmur involving systole and diastole was heard. This murmur was transmitted throughout the precordium. The pulmonic second sound was loud.

X-rays showed diffuse enlargement in all diameters, most marked of the left ventricle. The left border was straight and steep, and both lungs showed congestion which did not show "lular dance" on fluoroscopy. The superior mediastinum appeared broadened due to a prominent vena cava and ascending aorta, and in oblique views the pulmonary conus appeared prominent but not the left auricle. Electrocardiograms showed no significant changes, and electrostethograms showed a continuous irregular murmur present throughout systole and diastole, heard with greatest intensity at the pulmonary area and transmitted to the apex.

Operation on this admission was deferred because on Jan. 2, 1940, he developed an acute upper respiratory infection and on January 22, fever and deep jaundice, presumably catarrhal. This began to clear on January 29, and he was discharged to a convalescent home on Feb. 7, 1940.

He was readmitted to Bellevue Hospital on April 23, 1940, for ligation of his patent ductus. His condition was essentially unchanged except for some gain in weight and minimal evidence of respiratory infection.

Operation was done April 26, 1940. A ductus about 1 cm. in diameter and 5 mm. long was exposed and doubly ligated with heavy braided silk according to the technique of Gross. Intra-tracheal ether was used and the patient stood the procedure well.

Postoperatively he was comfortable though somewhat dyspneic for the first two days during which his temperature fluctuated up to 102°. On the second day x-ray showed evidence of pleural exudate and 550 c.c. of bloody fluid was withdrawn on thoracentesis. The following day 200 c.c. more were withdrawn. On the fourth day his temperature rose to 103.2°, he appeared acutely ill, and x-rays showed density of the midthird of the left lung and widening of the mediastinum. During the next forty-eight hours 9 Gm. of sulfapyridine were given and his temperature returned to normal, where it remained. On the seventh day he appeared slightly icteric, but his general condition had much improved. His wound had healed by primary union.

From Nov. 1, 1939, until Sept. 1, 1940, she was admitted and discharged four times due to difficulties related to her metatarsal anomalies. In October, 1940, an imperforate choana was corrected, and in 1941 her feet again required hospital care. During this period she grew rapidly in height and improved conspicuously in vigor though her nutrition was not well maintained at home. Her heart signs did not change, a short, soft systolic murmur was constantly heard at the base, and her blood pressure remained at 110/80. Because of the difficulties related to her feet, activity was somewhat restricted for much of this time, but there were periods of vigorous activity which caused no cardiac symptoms, nor evidence of decompensation.

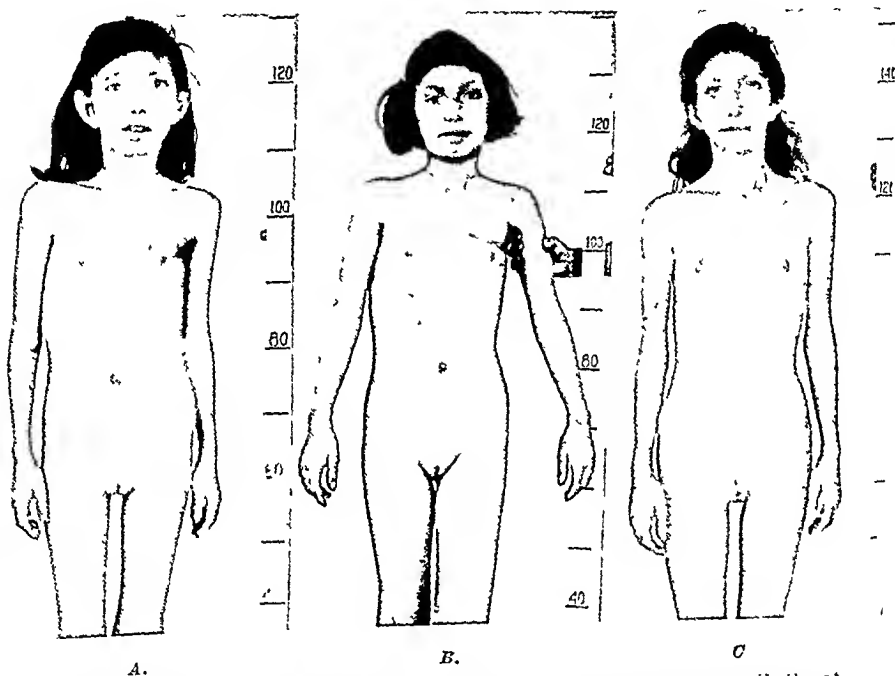


Fig. 3. Case 1—A, Ten days after operation, note poor nutrition, apathetic attitude, and expression. B, Six months after operation, note great improvement in nutrition and gain in height in spite of the fact that disease of the tarsal bones had kept her hospitalized. C, Two years after operation, note increase of 20 cm. in height though nutrition has not been well maintained. The left mammary gland is developing normally under the scar.

CASE 2.—R. B. was born at home on Sept. 15, 1928, a normal full-term delivery. He was the fourth of seven children of Italian parents. An older brother and a sister suffer from rheumatic heart disease and all members of the family became infected with trichina in 1934. Otherwise the siblings and parents are in good health.

His neonatal period passed uneventfully and he developed at a normal rate, though a diagnosis of congenital heart disease was made, because of a cardiac murmur, at the age of three months. He was followed in the cardiac clinic of the Nursery and Child's Hospital from this time until the age of four years when he was transferred to the Bellevue Hospital cardiac clinic.

During the next five years he was seen frequently with respiratory infections which on three occasions were of sufficient severity to require admission.

On Jan. 22, 1937, he was admitted because of fever, dyspnea, fatigue, joint pains, and general malaise. He appeared acutely ill, pale and slightly icteric, with

best in the second left interspace, but was plainly audible throughout the area of cardiac dullness as well as in the neck and along the spine.

X-ray for the first time showed a prominence in the area of the pulmonic conus. Electrocardiogram showed no abnormality and almost no change since that of 1933.

Operation was done June 25, 1940. A ductus about 0.8 cm. in diameter and 0.8 cm. long was doubly ligated according to the technique of Gross under intratracheal ether. No difficulty was encountered and the patient stood it well.

Postoperatively his immediate course was excellent. June 30, he was out of bed, and walking on July 2, with the wound apparently healed. However, he began showing fever on July 3, and by July 5, it was apparent that an infection of the wound was present. The wound was opened on July 7, releasing several cubic centimeters of thick pus culturing *Staphylococcus aureus hemolyticus* from the subcutaneous tissue. The pleura was not involved and the temperature returned to normal but the wound continued to drain small amounts of pus.

On Aug. 9, 1940, the wound was opened widely under general anesthesia. One large pericostal silk suture and several silk knots were removed. No evidence of infection in cartilage or pleura was found. The wound was packed open and he was discharged on Aug. 17, 1940. Examination at this time showed no murmur and blood pressure of 96/64. X-ray of heart showed no abnormality of contour.

On Sept. 6, 1940, he was readmitted because of fever and cough. Examination showed numerous moist râles and rhonchi in the left chest, fewer on the right. His heart showed no change on physical examination and there was no evidence of pleural fluid. X-ray of the heart at this time showed a more prominent pulmonary arterial shadow than before operation, possibly due to relative diminution in size of the left ventricular shadow. He was discharged on Sept. 28, 1940, with his chest clear.

In the dressing clinic his wound had healed by Oct. 7, 1940, and he was discharged to a convalescent home.

On Dec. 3, 1940, he had gained nine pounds over his preoperative weight and eleven over his weight on discharge. He had had no cardiac symptoms and appeared in excellent health. His heart sounds were slow, strong, and regular, with an exaggerated P_2 but no murmurs.

On Feb. 3, 1941, he had gained eight more pounds and was eating well without urging. He had had only one cold lasting two days, in marked contrast to his previous winters. His heart sounds were unchanged.

On June 6, 1941, he had continued in good health but had gained no more weight and had had another mild cold with cough. In August, 1941, he had another cold. However, his general vigor and health remained at a definitely higher level than before operation, he was eating well and beginning to develop sexually. His heart sounds remained free of murmurs.

CASE 4.—J. B. was born in the Swedish Hospital of Brooklyn in March, 1931, a breech delivery at full term. She was the second of three children of American parents. Both sisters and both parents are in good health and no familial diseases are known.

Her neonatal period passed uneventfully, feeding being by cow's milk formula with adequate vitamins added from the start. She was always rather small and thin but was not retarded in walking or talking. At no time did she have any spells of cyanosis. At 2 years of age her tonsils and adenoids were removed because of frequent colds. At three years, following a severe case of measles, a heart murmur was found to be present. This murmur was unassociated with any cardiac symptoms other than mild dyspnea and palpitation on exertion. She did not receive any treatment for her heart, nor was she restricted in activity at school, but she was always small and thin for her age and subject to frequent respiratory infections.

On the tenth day he was given a transfusion of 250 cc and this was repeated on the twelfth day, as his blood count remained at 2,400,000. Following this he improved steadily and by the eighteenth day was walking. X rays during the fourth week showed some persistent atelectasis or fluid in the left lung field, as well as widening of the mediastinal shadow, but he felt increasingly well, and auscultation and electrostethogram showed no evidence of the previously present murmurs. He was discharged, weighing 93 pounds, on his twenty seventh postoperative day, May 23, 1940.

During June he remained apprehensive in attempting activity and was sent to the posture clinic for correction of a scoliosis acquired postoperatively. During the summer he was allowed full activity in a boys' camp where he found that his previous limitations on exertion were no longer present, and made a striking improvement in nutrition and vigor.

On Oct 10, 1940, he had gained thirteen pounds and grown one inch in the five months since operation. His heart shadow on x ray was normal in size and contour, and examination revealed no murmur. He was able to keep up with normal children in active play without signs of dyspnea or fatigue.

One year after operation he had gained another three pounds and another inch. He was leading an entirely normal life.

CASE 3—F F was born in Harlem Hospital on Oct 8, 1928, a normal full term delivery. He was the first of three children of Puerto Rican parents. An extensive hemangioma involving one arm is present in one sister, otherwise both parents and siblings are in good health and no familial diseases are known.

His neonatal period was uneventful and he gained weight and developed normally during the first fifteen months, being breast fed for this period. At ten months he was examined by a doctor because of a respiratory infection and a heart murmur was found. During the second year he seemed to tire easily at play and had frequent respiratory infections. Cyanotic spells were absent.

On Oct 18, 1930, he was admitted to Babies Hospital with signs of chronic bronchitis and a heart enlarged to percussion with a very loud continuous harsh murmur in the left second interspace, transmitted to the back. There was some asymmetry of the chest with prominence just to the left of the sternum. In spite of a great deal of violent screaming, no cyanosis was present. X ray of the chest showed cardiac enlargement only, electrocardiogram was negative, blood pressure 90/40. He was followed at irregular intervals in the cardiac clinic where it was noted that he tended to remain underweight and to have many colds.

During the next six years he was admitted to Babies Hospital on four occasions, once because of a gangrenous appendix, once for a severe respiratory infection, once for intestinal obstruction, and finally for tonsillectomy in the hope of relieving his frequent respiratory infections.

In 1937 his failure to gain weight became a difficult problem because of the emotional instability of his parents. Mild frequent colds continued. During 1938 and 1939, he improved and was in fair condition. The precordial bulge and thrill, the coffee mill murmur in the pulmonary area, and the slight cardiac enlargement persisted, but he was able to shift from a special cardiac class to a prechival school where he got along well without physical restrictions.

He was admitted to Babies Hospital for ligation of the patent ductus on June 22, 1940. Examination showed Temperature, 101°, pulse, 96, respirations, 29; blood pressure, 110/70, height, 4 feet 8 inches; weight, 71 pounds. He was a swarthy boy of asthenic habitus who, except for his chest, showed no abnormalities other than two well healed abdominal scars. His heart was enlarged to 2 cm beyond nipple line on left. Precordial bulge of the chest was apparent and a definite thrill and fro thrill was easily felt. The loud systolic and diastolic murmur was heard

best in the second left inter-space, but was plainly audible throughout the area of cardiac dullness as well as in the neck and along the spine.

X-ray for the first time showed a prominence in the area of the pulmonic cone. Electrocardiogram showed no abnormality and almost no change since that of 1933.

Operation was done June 25, 1940. A ductus about 0.8 cm in diameter and 0.8 cm long was doubly ligated according to the technique of Gross under intratracheal ether. No difficulty was encountered and the patient stood it well.

Postoperatively his immediate course was excellent. June 30, he was out of bed, and walking on July 2, with the wound apparently healed. However, he began showing fever on July 3, and by July 5, it was apparent that an infection of the wound was present. The wound was opened on July 7, releasing several cubic centimeters of thick pus culturing *Staphylococcus aureus hemolyticus* from the subcutaneous tissue. The pleura was not involved and the temperature returned to normal but the wound continued to drain small amounts of pus.

On Aug 9, 1940, the wound was opened widely under general anesthesia. One large pericostal silk suture and several silk knots were removed. No evidence of infection in cartilage or pleura was found. The wound was packed open and he was discharged on Aug. 17, 1940. Examination at this time showed no murmur and blood pressure of 96/64. A ray of heart showed no abnormality of contour.

On Sept. 6, 1940, he was readmitted because of fever and cough. Examination showed numerous moist râles and rhonchi in the left chest, fewer on the right. His heart showed no change on physical examination and there was no evidence of pleural fluid. X ray of the heart at this time showed a more prominent pulmonary arterial shadow than before operation, possibly due to relative diminution in size of the left ventricular shadow. He was discharged on Sept. 28, 1940, with his chest clear.

In the dressing clinic his wound had healed by Oct. 7, 1940, and he was discharged to a convalescent home.

On Dec. 3, 1940, he had gained nine pounds over his preoperative weight and eleven over his weight on discharge. He had had no cardiac symptoms and appeared in excellent health. His heart sounds were slow, strong, and regular, with an exaggerated P₂ but no murmurs.

On Feb. 3, 1941, he had gained eight more pounds and was eating well without urging. He had had only one cold lasting two days, in marked contrast to his previous winters. His heart sounds were unchanged.

On June 6, 1941, he had continued in good health but had gained no more weight and had had another mild cold with cough. In August, 1941, he had another cold. However, his general vigor and health remained at a definitely higher level than before operation, he was eating well and beginning to develop sexually. His heart sounds remained free of murmurs.

CASE 4—J. B. was born in the Swedish Hospital of Brooklyn in March, 1931, a breech delivery at full term. She was the second of three children of American parents. Both sisters and both parents are in good health and no familial diseases are known.

Her neonatal period passed uneventfully, feeding being by cow's milk formula with adequate vitamins added from the start. She was always rather small and thin but was not retarded in walking or talking. At no time did she have any spells of cyanosis. At 2 years of age her tonsils and adenoids were removed because of frequent colds. At three years, following a severe case of measles, a heart murmur was found to be present. This murmur was unassociated with any cardiac symptoms other than mild dyspnea and palpitation on exertion. She did not receive any treatment for her heart, nor was she restricted in activity at school, but she was always small and thin for her age and subject to frequent respiratory infections.

She was admitted to Babies Hospital on Sept. 9, 1940, for ligation of the patent ductus. Examination showed: Temperature, 99°; pulse, 90; blood pressure, 114/64; height, 4 feet 2 inches; weight, 50¾ pounds. She appeared puny but in good health and, aside from her heart, showed no abnormalities other than a right ptosis with asymmetry of the face and a tendency to hold the head off center without showing definite torticollis. Her heart was not enlarged and there was no precordial bulge. A mild thrill was present at the base, where a loud, harsh, crescendo systolic and diastolic murmur replaced the heart sounds. At the apex the sounds were of good quality and the murmurs could be heard only faintly in systole. The murmur was transmitted to the back and neck, but there was no "pistolshot" in the groin, no capillary pulsation in the nail beds, and no clubbing of the fingers.

X-rays of the chest showed a cardiac shadow which was normal in contour. Roentgenkymograph and fluoroscopy failed to show abnormal pulsations. Electrocardiogram was normal and electrostethogram showed a murmur characteristic of patent ductus.

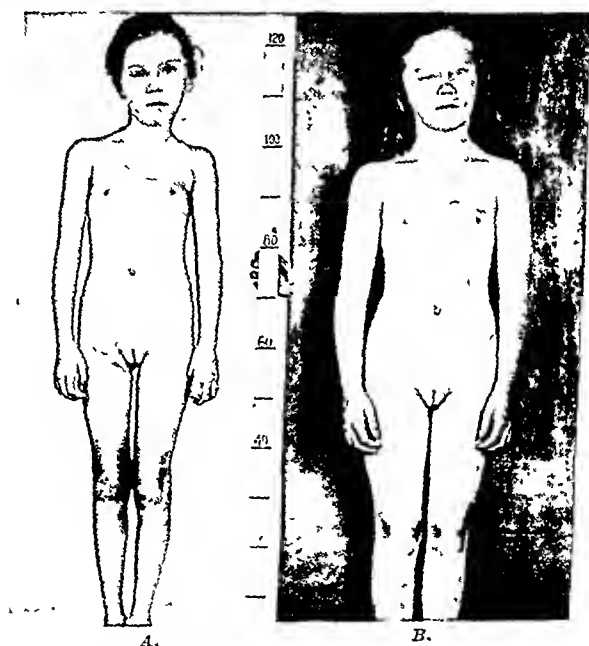


Fig. 4, Case 4.—A, One week after operation. The patient is small and thin but not markedly malnourished, torticollis is probably related to squint. B, Six months after operation. The gain in nutrition and vigor is obvious, not demonstrated is a considerable gain in height. Even the torticollis seems less conspicuous.

Operation was done Sept. 24, 1940. A small open ductus, about 0.8 cm. long and 0.4 cm. in outside diameter was found and ligated doubly according to the Gross technique, under endotracheal ether.

Postoperatively she did very well. On the first day her temperature reached 100°, thereafter remaining flat. She was up in a chair on the third day and walking on the sixth, when her stitches were removed, the wound being cleanly healed. The murmur heard preoperatively was completely absent on auscultation and on sound tracings taken on October 3. She was discharged on October 15, to a convalescent home.

On Nov. 18, 1940, she had gained eight pounds in the eight weeks since operation. She had no cardiac symptoms.

On Feb. 3, 1941, there had been no further gain in weight due to a recent respiratory infection, but she had grown in height and was able to exercise with much less fatigue than previously.

On May 5, 1941, she weighed 61 pounds and measured 51 inches, a gain of eleven pounds and two inches in the eight months since operation. She had been far more active than ever before and this activity had caused less fatigue than usual. She was aware that sensations of palpitation and discomfort previously present in her chest on exertion were absent. Heart sounds still showed a somewhat accentuated P_2 but no murmur.

CASE 5—T. X. was born at home on July 14, 1928, a normal full term delivery. He was the fifth of nine children of American parents of German ancestry. A paternal aunt died in late adolescence due to congenital heart disease. Both parents and all eight siblings are in good health and no other familial disease is known.

He is said to have been a "blue baby" and to have remained more or less cyanotic for the first eight months of his life, after which cyanosis appeared intermittently in relation to exercise and also to cold damp weather. A loud cardiac murmur was recognized at birth. In spite of this he took artificial feedings well and developed at a normal rate. Respiratory infections were fairly frequent but never prolonged or severe. Exertion always caused dyspnea and he found it easier to breathe at night by elevating his head with two pillows. His shortness of breath caused him to tire rapidly and led to his placement in a special cardiac class at school. His weight and size were always less than his siblings at comparable age.

He was admitted to Babies Hospital on Dec. 30, 1940, for ligation of the patent ductus. Examination showed: Temperature, 99.6° , pulse, 88, respirations, 28, blood pressure, 130/45 with sounds still audible at zero; height, 4 feet 4 inches, weight, 57 pounds. He was a poorly developed little boy looking younger than 12 years of age, alert and cooperative and showing apparent pallor without cyanosis, but no evidence of acute illness. His fingers showed capillary pulsation in the nail beds, but no clubbing. His thorax was long and narrow with a definite though slight precordial bulge. His heart was enlarged to percussion. The apex impulse was clearly visible in the fifth interspace in the anterior axillary line and over the base a marked thrill was felt, most easily over the second left interspace where a long, loud, harsh systolic murmur was heard. This was transmitted throughout the cardiac area and into the neck and back. There was no diastolic murmur. Over the great vessels of the arms and legs a "pistolshot" systolic sound was present. The liver and spleen were not palpable and the remainder of the examination revealed no remarkable abnormalities.

X rays showed a prominent pulmonary conus, enlargement of the heart to the left, and very marked increase in the caliber of the pulmonary vessels which showed conspicuous pulsation on fluoroscopy. Electrocardiogram showed no important findings and electrostethogram showed a long systolic murmur at the third left interspace and aortic area with short early diastolic murmurs, in addition, at the apex and pulmonary area.

Operation was done Jan. 9, 1941. A large ductus, about 2 cm in diameter, was exposed and ligated with a single heavy silk ligature. The mediastinum appeared edematous and contained several large lymph nodes and dilated veins in the region of the ductus. Because of mediastinal bleeding a second ligature was not used, but bleeding was apparently controlled before closure. Intratracheal ether was used.

Postoperatively he became very restless and excited on recovery from anesthesia and in spite of a heavy sedative, thrashed about a great deal. He showed no respiratory distress for the first forty-eight hours, after which he developed dyspnea and evidence of fluid in the left chest. Thoracentesis at this time yielded 400 cc. of bloody fluid. By the fifth day his temperature was normal but a severe epistaxis had resulted in pallor and prostration. The following day a murmur was found to

have reappeared, at first diastolic only but later more nearly continuous than before operation. In spite of this, his recovery continued without interruption. His wound was completely healed on the seventh day and he was allowed up on the ninth day. He was discharged on Jan. 23, 1941.

On February 3 he showed little change, his weight being the same as before operation and the nearly continuous murmur still present. X-rays of the chest showed some reduction in size of the superior mediastinal shadow and of the pulmonary conus, but still a grossly enlarged cardiac shadow.

On March 24, he still showed no striking improvement. He had had a fever of 103° the previous week, attributed to a sore throat. His chest signs were unchanged.

On April 28, the murmur seemed louder than before and for the first time since operation was accompanied by a thrill. He had been out of school for the preceding month because of fever attributed to respiratory infection.

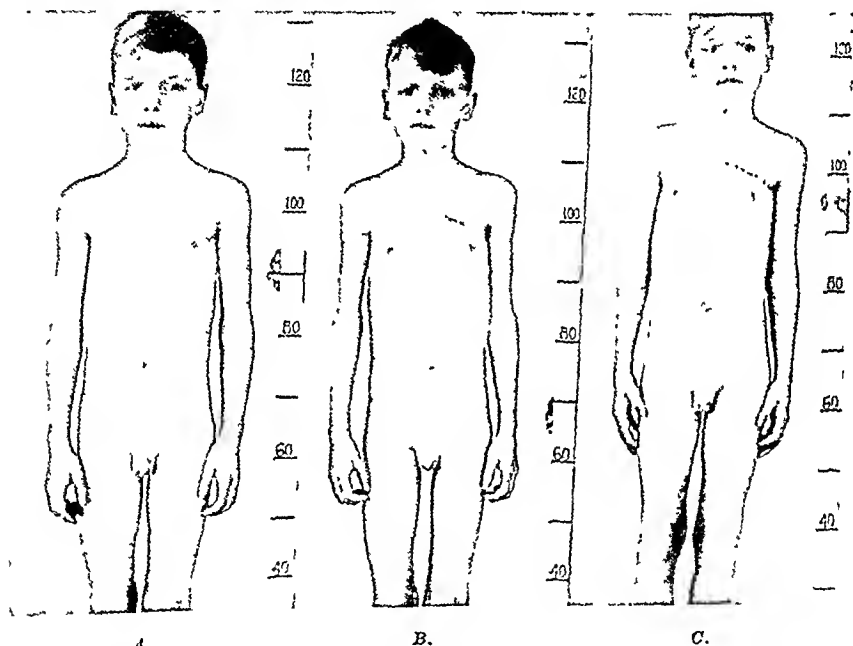


Fig. 5. Case 5—A, Before operation. Nutrition is fairly good but the patient is very small and undeveloped for a boy of twelve years. B, Four months after the first operation. At this time the patency had recurred and he had had a positive blood culture for over a month. He is beginning to show emaciation. C, Two months after second operation. He is now better nourished and even a little taller than before the first operation. Improvement in these two months is conspicuous.

On May 6 he was readmitted to Babies Hospital for consideration of reoperation. Examination at this time showed: Temperature, 100.2° ; pulse, 100; respirations, 36; blood pressure, 120/0; height, 4 feet 4 inches; weight 53 pounds. He was paler and thinner than on his first admission and somewhat dyspneic but still alert and cooperative. His heart was conspicuously enlarged with the point of maximum impulse in the anterior axillary line, sixth interspace. A precordial thrill was present after activity and absent at rest, but the pulmonary second sound could be palpated at all times. A loud, rough systolic murmur continuous with a softer diastolic was best heard under the well-healed scar over the second left interspace and was transmitted to the apex as well as to the back. Some tenderness and resistance was present over the liver, which could be felt two fingers below the costal

margin. The smooth, nontender spleen was readily felt four fingers below the costal margin. Capillary pulsation and "pistolshot" in the groin were again noted.

X-rays showed an enlarged heart with prominent pulmonary arterial shadow as well as conspicuous pulmonary bronchovascular shadows. The findings were less conspicuous than before operation. Electrocardiogram showed no significant changes. Electrosthethogram showed a continuous murmur throughout the cardiac cycle.

Preoperatively he showed the presence of a hemolytic *Staph. aureus* on every blood culture. His fever varied up to 104.6° for the first week, during which sulfathiazole was given in increasing amounts. During the second week fever was lower with occasional spikes, while he was getting 4.5 Gm. of sulfathiazole a day. Because this resulted in a blood level of only 3 mg. per cent the dose was gradually increased to as much as 12 Gm. a day. By May 27, his blood contained 10 mg. per cent and his fever had disappeared, but the onset of toxic symptoms characterized by vomiting and severe leucopenia made it necessary to stop administration of the drug. Since organisms were still present in his blood, after a week without drug, sulfadiazine was begun. For the next three weeks, 6 Gm. a day were given, during which time his blood level varied from 6 to 10 mg. per cent. In spite of this,

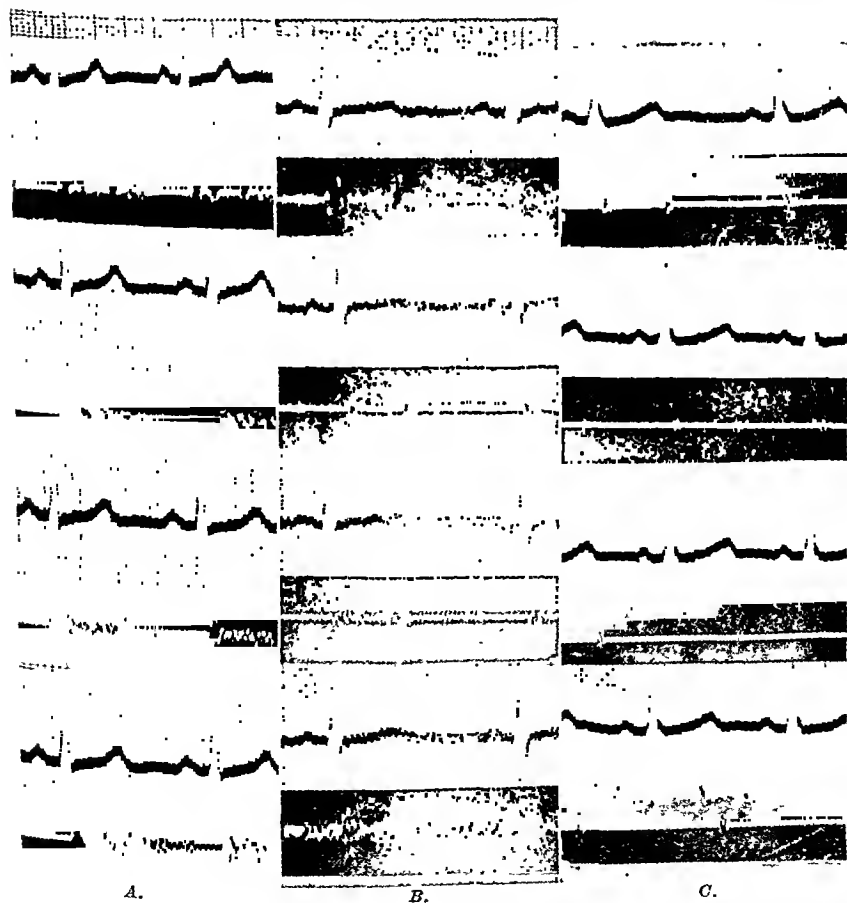


Fig. 6.—Stethograms of Case 5; apical, third left interspace, aortic arch, and pulmonic areas, from top to bottom. A, Before operation; systolic murmur at all stations with an early diastolic at the apex and pulmonic areas. B, One month after first operation; at all stations there are systolic and diastolic murmurs, being maximum in the pulmonic area. C, One month after second operation; the murmurs are no longer present.

organisms persisted in the blood stream and fever reappeared. On June 19, anti-staphylococcus immune rabbit serum,* 40 c.c. was given intravenously with an immediate temperature reaction to 105.6°, followed by a drop to 96° and a secondary rise to 104° within twelve hours. Throughout this preoperative period he had shown no petechiae or other peripheral embolic symptoms, but on frequent occasions complained of chest pain which was often accompanied by exacerbation of fever, and sometimes by transient pleural rubs. Cough and sputum were absent.

Reoperation was done June 24, 1941. The ductus was found wide open with a diameter of about 1.5 cm. and a considerably thicker wall than before. No trace of the heavy ligature was seen, though the former fine black silk ties were readily seen in the mediastinal scar. A double ligature of umbilical tape was used, with immediate elimination of the thrill, and 3 Gm. of sulfathiazole crystals were spread through the exposed mediastinal tissues.

Postoperatively his immediate reaction was good until twenty-four hours after operation, when his temperature reached 104° and he appeared prostrated. Dullness, bronchial breathing, and many fine râles developed over the left base and were considered to be due to atelectasis. On the second day sulfadiazine treatment was resumed and continued for seven days during which his chest signs slowly cleared, his temperature returned to normal, and his wound healed by primary union. A blood culture taken on the operating table grew hemolytic *Staph. aureus*. The first culture thereafter was taken on June 30, six days after operation; it failed to show growth. Four cultures taken during the following eight weeks were all sterile. On the tenth day, because sulfadiazine could not be obtained, the patient was given 2 Gm. of sulfathiazole. That evening his temperature suddenly rose to 104.4° and remained between 102° and 106° for three days, gradually falling to normal six days later. This was considered to be a drug reaction and no further medication was given. During the third, fourth, and fifth weeks after operation his temperature remained normal with occasional transient episodes of fever. His heart sounds were clear, without murmurs, his pulse quiet, and his diastolic pressure was maintained. His chest signs cleared entirely, though some density remained on x-ray and the shadow of his heart changed little. Electrocardiogram, which had shown an inversion of T₄F, returned to normal. Electrosthethograms showed inconstant faint systolic murmurs which could not be verified on auscultation. Blood cultures remained negative. His activity increased slowly and he began to gain weight. By the sixth week he was walking, had gained eight pounds, no longer showed a palpable spleen, and seemed in excellent health. On August 22, he was discharged, fifty-nine days after operation, to a convalescent home.

On Oct. 20, 1941, his excellent health had been maintained. He had gained six more pounds and was able to return to school without disability. His heart sounds showed no murmur, his heart shadow by x-ray being smaller than at any time since first examined, but still showing a prominent pulmonary arterial bulge.

CASE 6.—R. H. was born at home on March 10, 1930, a normal full-term delivery. He was the second of three children of American parents. His older sister and younger brother are both in good health and show no congenital defects, and both parents are in good health. There is no history of cardiac disease or other familial illness in grandparents or parent's siblings.

His neonatal period was somewhat complicated by difficulty in feeding. Several formulas were used but he took them all poorly and gained only slowly. He had no cyanotic spells, but from earliest infancy a rapid and conspicuous cardiac pulsation had been noted which could also be seen in his neck. In spite of these difficulties he developed at a normal rate.

On May 11, 1934, he was first seen in Babies Hospital clinic because of a cold, cough, and fever of two weeks' duration. At this time examination showed a poorly

*Lederle Laboratories, Inc.

nourished child with a skull suggesting rickets, congested conjunctivae, inflamed pharynx, and thickened eardrums. There was a marked pulsation, visible in the neck, and a precordial pulsation visible beyond the nipple line, where a pronounced thrill could be felt. A loud rough systolic murmur was heard all over the precordium, greatest in the third left interspace, and the pulmonary second sound was increased. Blood pressure was 140/80. X-ray showed a markedly enlarged cardiac shadow, the outlines of which were confused by densities at both pulmonary hilae suggesting pulmonary congestion or tuberculosis. Tuberculin was negative.

During the next six years he was seen at the clinic at irregular intervals. He grew slowly and remained consistently underweight. He was subject to frequent respiratory infections, on one occasion had an epistaxis which required packing, and had bronchopneumonia at 5 years of age. An x-ray in 1937 showed cardiac enlargement and a prominent pulmonary arterial shadow, as well as exaggerated bronchovascular markings. Electrocardiogram showed slurred QRS complexes throughout. His diastolic pressure fell slowly as he grew but his murmur remained primarily systolic. He was very active, in spite of which he was placed in a cardiac class in school. During the winter of 1940 he contracted a severe bronchitis which kept him at home for long periods, during which time he failed to gain weight, so that his parents became willing to accept surgical intervention which had been suggested in the autumn.

He was admitted to Babies Hospital on May 5, 1941, for study, preparatory to ligation of the ductus. Examination showed: Temperature, 100°; pulse, 96; blood pressure, 116/40; height, 4 feet 5 inches; weight 55 pounds. He was a small, thin, overactive boy, very alert and cooperative. Aside from harsh breath sounds at the left base with occasional rhonchi, there were no significant abnormalities other than those related to the heart. There was no precordial bulge, but a marked visible and palpable systolic thrill was present over the entire precordium. The maximum apex impulse was felt in the anterior axillary line, sixth interspace, with the heart percussing correspondingly enlarged. A loud harsh systolic murmur heard with greatest intensity over the third left interspace was transmitted throughout the precordium, over the cervical vessels, and through to the back. An accompanying soft diastolic murmur was not transmitted. The pulmonary second sound was so loud it could be palpated. Though the pulse was of Corrigan type there was no true capillary pulsation or "pistolshot" in the groin. No clubbing or cyanosis was present.

X-rays showed all of the roentgen criteria necessary for a diagnosis of patent ductus arteriosus. They also demonstrated the presence of an anomalous hemivertebra in the thoracic spine. Electrocardiogram showed no important findings and electrostethogram confirmed the auscultatory findings.

Operation was done June 10, 1941. A thick-walled ductus 1.5 cm. in diameter was exposed and doubly ligated with woven cotton umbilical tape, under endotracheal ether.

Postoperatively his temperature rose to 101° on the first day, subsiding to normal after the fourth. There were signs of patchy atelectasis over the left base which gradually cleared during the first week. He was allowed up on the seventh day at which time his sutures were removed, the wound being healed by primary union. At this time, though his pulse was slower and heart action quieter than before operation, a definite continuous murmur was again heard in the third left interspace, with transmission of the systolic element to the apex and aortic areas, but with no accompanying thrill. On the eleventh day he was discharged home.

On June 30 he had changed very little in the week since discharge, with the murmur conspicuously present but without accompanying thrill. He seemed in excellent condition, very active and alert, but had gained no weight. X-rays at this time showed no change in cardiac contour.

On Oct. 20, 1941, he had gained only four pounds in the four months since operation. His general condition appeared to have changed very little and he still showed

a conspicuous continuous murmur under the scar of his operation, the systolic element of which was transmitted to the base and aortic area. His blood pressure remained at 106/60.

CASE 7.—J. M. was born at the Summit Hospital on June 7, 1930, a normal full-term delivery. He was the oldest of three children of American parents. A brother drowned at 3 years of age, a sister six years old is living and well, as are both parents. As far as is known no other familial disease exists in the family of either parent.

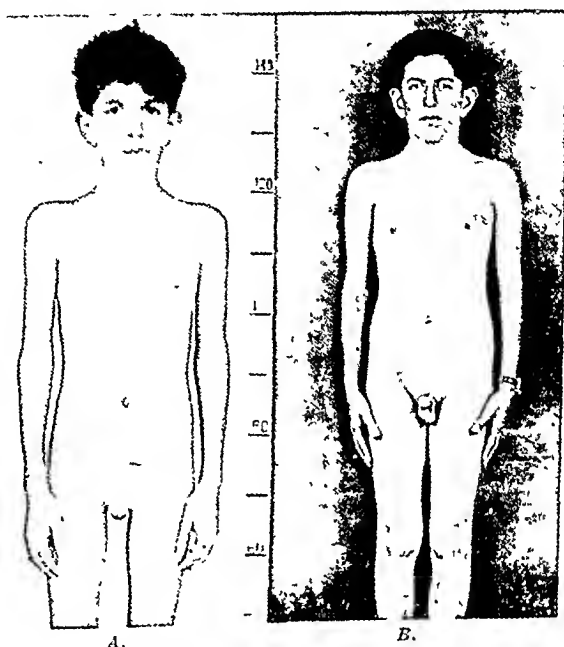


Fig 7, Case 7.—A, Before operation. Poor nutrition is evident, at this time the patient had been running a positive blood culture for over a month. B, Two months after operation; marked improvement in nutrition and vigor is apparent.

His neonatal period passed uneventfully, with no retardation of development and normal growth on an adequate diet. When he was 13 months of age, a cardiac murmur was first noted, but there were no cyanotic spells or other evidence of disturbed function. His rate of growth and development were within normal limits, and it was not felt necessary to restrict his physical activity. It is probable, however, that exertion was more fatiguing to him than to his contemporaries, as he tended to avoid physical contests and became socially somewhat seclusive. He did not appear to be chronically ill, nor did he suffer from repeated respiratory infection. When he was 10 years old, because of faulty posture, spinal x-rays were taken which showed a faulty development of the bodies of most of the thoracic vertebrae, thought to be congenital in origin. Back exercises were prescribed.

On June 8, 1941, he complained of pain in both hips and the left knee, which showed some redness and swelling. He was found to have a fever of 103°, and three days later a typical measles rash appeared. The joint pains were transitory and trivial and the fever subsided to 101° after the appearance of the rash, but persisted intermittently after the rash had disappeared.

On June 28, 1941, he was admitted to Overlook Hospital because of continued fever, anorexia, and weakness. Two successive blood cultures at four day intervals grew *Streptococcus viridans*. Sulfathiazole by mouth was begun on July 4, 1941.

He was transferred to Babies Hospital on July 8, 1941, for consideration of further treatment. Examination showed: Temperature, 100.6°, pulse, 94 respirations, 30; blood pressure, 136/50; height, 1 foot 8½ inches, weight 71 pounds. He was a fairly well developed and nourished boy of eleven, asthemic in habitus and round shouldered in posture, but not appearing acutely ill. There was slight pallor but no cyanosis and his skin was free of rash or petechiae. His thorax was thin and free of deformity other than a slight exaggeration of the spinal kyphosis. His heart was not enlarged; its pulsation was conspicuous, with maximum impulse on the fifth interspace, 6 cm. from the mid sternal line, there was no definite thrill. A loud, systolic, swishing murmur was heard throughout the precordium but loudest in the third left interspace where a softer diastolic component was also present. The pulmonary second sound was accentuated. The systolic murmur was transmitted to the brach, but there was no "pistol-shot" in brachial or femoral arteries and no capillary pulsation in the nail beds. Liver and spleen were not palpable and no other abnormalities were noted.

X rays showed a heart shadow within normal limits of size and shape except for a suggestive bulge in the region of the pulmonary cone. The lungs were clear and showed no conspicuous bronchovascular markings. Electrocardiogram showed only tachycardia, and electrostethogram showed systolic and diastolic murmurs in all leads.

Preoperatively he showed the presence of a *Strep. viridans* on seven successive cultures including one taken on the operating table. Sulfathiazole was continued at the rate of 3 Gm. a day for the first ten days. During this time his temperature showed daily swings to 102° and he became slightly cyanotic and nauseated. After a week without medication during which his fever did not change, he was given 500 cc of blood in two transfusions, and sulfapyridine was begun at the rate of 3 Gm. daily. This resulted in a good deal of nausea but during the following two weeks his fever gradually flattened to a daily rise to about 100°. During this time his blood contained 6 mg per cent of sulfapyridine and continued to grow streptococci on culture.

Operation was done Aug. 8, 1941. A ductus about 0.9 cm in diameter and 1.2 cm. long, with a fairly thin wall, was found. The surrounding mediastinum was somewhat edematous, and an enlarged lymph node which lay directly over the ductus showed Gram positive cocci on smear. Two ligatures of umbilical tape were used to close the ductus. Sulfathiazole crystals, 3 Gm, were placed in the exposed mediastinal tissues.

Postoperatively he reacted very well. His temperature rose to 101° on the first day but reached normal on the second, where it remained. Sulfapyridine was given from the second to the seventh postoperative day, by which time his wound had healed by primary union. There was never any evidence of postoperative pneumothorax or atelectasis and no murmurs could be heard. A blood culture taken on the operating table grew *Strep. viridans*. The first culture thereafter was taken on August 11, three days after operation, it failed to show growth, as did one taken ten days, and a third, two weeks, after operation. On the seventh day he was allowed up and he began walking on the tenth. His appetite, vigor, and disposition improved dramatically during the second week. X rays at this time showed little change in the cardiac shadow, electrocardiograms showed increase in amplitude of the T waves, and electrostethograms showed a persistent soft systolic murmur at the apex which could not be verified on auscultation. On August 28, twenty days after operation, he was discharged.

On September 29, he had gained eighteen pounds since before operation and was two inches taller than before his illness. His appetite for the first time was hearty, and he appeared and behaved more vigorous than before his acute illness. He had had no fever and no cardiac symptoms, and his heart sounds were strong, quiet, and free of murmurs.

a conspicuous continuous murmur under the scar of his operation, the systolic element of which was transmitted to the base and aortic area. His blood pressure remained at 106/60.

CASE 7.—J. M. was born at the Summit Hospital on June 7, 1930, a normal full-term delivery. He was the oldest of three children of American parents. A brother drowned at 3 years of age, a sister six years old is living and well, as are both parents. As far as is known no other familial disease exists in the family of either parent.

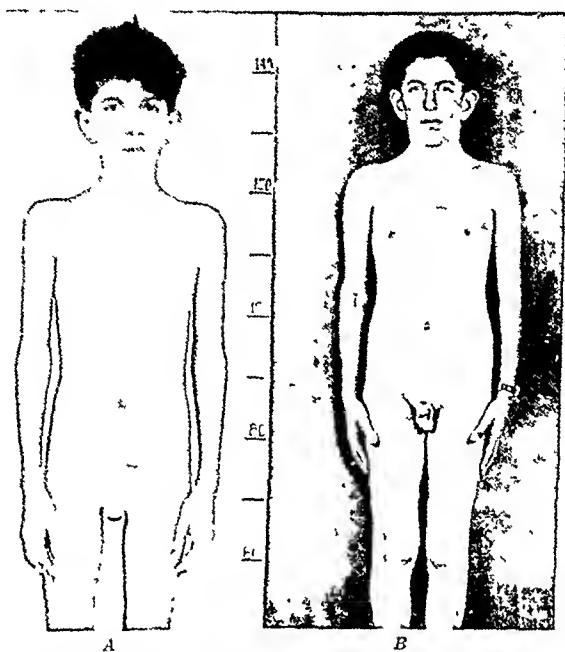


Fig. 7, Case 7.—A, Before operation. Poor nutrition is evident at this time the patient had been running a positive blood culture for over a month. B, Two months after operation marked improvement in nutrition and vigor is apparent.

His neonatal period passed uneventfully, with no retardation of development and normal growth on an adequate diet. When he was 13 months of age, a cardiac murmur was first noted, but there were no cyanotic spells or other evidence of disturbed function. His rate of growth and development were within normal limits, and it was not felt necessary to restrict his physical activity. It is probable, however, that exertion was more fatiguing to him than to his contemporaries, as he tended to avoid physical contests and became socially somewhat seclusive. He did not appear to be chronically ill, nor did he suffer from repeated respiratory infection. When he was 10 years old, because of faulty posture, spinal x-rays were taken which showed a faulty development of the bodies of most of the thoracic vertebrae, thought to be congenital in origin. Back exercises were prescribed.

On June 8, 1941, he complained of pain in both hips and the left knee, which showed some redness and swelling. He was found to have a fever of 103°, and three days later a typical measles rash appeared. The joint pains were transitory and trivial and the fever subsided to 101° after the appearance of the rash, but persisted intermittently after the rash had disappeared.

On June 28, 1941, he was admitted to Overlook Hospital because of continued fever, anorexia, and weakness. Two successive blood cultures at four day intervals grew *Streptococcus viridans*. Sulfathiazole by mouth was begun on July 4, 1941.

the diagnosis can be made, but who show little effect on their general health. It is uncertain whether the extra cardiac load is great enough in them to warrant the risks involved in eliminating it.

Both of the reported postoperative deaths were associated with infection, and the unsuccessful result of the first operation in Case 5 of this series was also associated with a complicating infection. Is the presence of infection in or near the ductus, then, a contraindication to operation? On the other hand, is the possibility of the eventual development of such infection a sufficient indication for operation even when the mechanical effects seem mild? This is the point of view held by Jones, Dolley, and Bullock. It is apparently supported by the fatal result in Streider's case, and by the two fatalities reported by Touroff and Vesell.¹⁶ On the other hand their first case,¹⁵ though also a near fatality on the table, has remained free of disease over a year after recovery, and three subsequent cases, operated upon by the same surgeon, are also apparently cured.¹⁷ Similarly, other cases ligated by Gross,¹⁸ and by Bourne and his associates,²² in the presence of subacute blood stream infection have remained free of infection postoperatively. In this series, the second operation on Case 5 and that on Case 7 seem to confirm the evidence that even an established subacute blood stream infection which has resisted intensive chemotherapy may be overcome by ligation of the duct.

Whether ligation of a patent ductus will prevent the formation of an infected thrombus near its site cannot be determined with certainty until a large number of ligated cases have been carefully followed for a long period. Though it seems reasonable to believe that infection may be prevented in this way, since the incidence of complicating infection is not certain, and since infection apparently may be overcome by prompt operation even after its occurrence, there is not yet sufficient evidence to warrant operation in every diagnosed case. For the present the operation is clearly indicated only if the patient shows evidence of mechanical overloading of the heart either by diminished cardiac reserve, by failure to grow and develop normally, by failure to maintain normal nutrition and resistance to infection, or if the ductus has become associated with an infected intimal thrombus with subacute blood stream infection.

SUMMARY

The results of eight instances of ligation of a patent ductus arteriosus in seven patients are reported. In six instances the ligation was carried out because of evidence of systemic effects of the mechanical circulatory abnormality. In two instances the ligation was carried out in order to overcome subacute bacterial blood stream infection which had resisted adequate chemotherapy with sulfonamide drugs.

No patient died following operation. In four instances the operation was conspicuously effective in overcoming the patient's mechanical circulatory symptoms. This improvement has been maintained for twenty-

On Oct. 22, 1911, he had gained four more pounds, was back at school carrying on with full activity. He had had no further fever and his cardiac signs were unchanged.

DISCUSSION

Sporadic attempts to ligate large blood vessels within the chest for the purpose of controlling hemorrhage have probably been made since the dawn of surgery. Such heroic efforts as Valentine Mott's,¹ over a century ago, even though *successful in securing the vessel without opening the pleura*, were doomed to failure because of infection. Undoubtedly this record contributed to the reluctance of surgeons to accept the suggestion made in 1907, by Munro,² even after aseptic surgery was well established, that a patent ductus arteriosus might be ligated. The first serious attempt was not reported until thirty years later when Graybiel and Strieder³ recorded their failure due to hemorrhage in an adult with subacute bacterial endarteritis, an experience shared though not recorded by others. Gross's⁴ success the following year resulted from his development of a new, deliberately transpleural, approach which enabled him to work out the technique of careful dissection⁵ by which all subsequently reported ligations, including those reported here, have been done.

What, then, can be accomplished by this procedure? In a series of papers Gross and co-workers have recorded their experiences,^{7, 8, 13} which they have summarized in a report of thirteen cases.¹⁰ All of these cases were selected according to the indications worked out by Hubbard, Emerson, and Green.⁶ One died, one, who has another vascular anomaly, has shown little change, and the remainder have shown gratifying and obvious improvement. Similarly, in the thirteen cases reported by Jones, Dolley, and Bullock,²⁰ *with the exception of one fatality, the results were good* though it is not clear in how many improvement was as conspicuous as in Gross's cases, or in those reported here. This may be due to the fact that these men have not been reluctant to urge operation on patients in whom the diagnosis was clear, but in whom general effects were not conspicuous, because of their conviction of poor prognosis due to ultimate blood stream infection.⁹ Both Gross and Jones have carried out a considerable number of ligations since their last publications. Other ligations or attempts at ligation have also been reported recently by Miangolarra and Hull,²¹ and still others have not yet been published.

It is clear that a patent ductus can be successfully obliterated by the method of Gross, and that this operation, carefully performed, is not one of great risk. If the mechanical effects of the presence of a patent ductus are as great as is indicated by the studies of Burwell, Eppinger, and Gross,^{11, 14, 20} it would seem that an operation of comparatively little risk should be considered seriously in every case where the diagnosis is reasonably certain. On the other hand, their studies were carried out on Gross's patients, in whom the ductus was of such size as to cause definite clinical effects, and on animals in which a comparatively large shunt had been produced experimentally. There are many patients in whom

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AN EXPERIMENTAL STUDY OF SHOCK WITH SPECIAL REFERENCE TO ITS EFFECT ON THE CAPILLARY BED*

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THE loss of circulating fluid with the corresponding decrease of volume of blood has long been known to be an important factor in the condition of secondary shock. Interest has centered on the capillary bed as a site where the fluid is lost. In this study the hepatic and mesenteric capillaries of the rat, under normal conditions, were compared with the capillaries of animals in which traumatic shock had been produced experimentally by different means in an attempt to obtain more exact knowledge of the capillaries in shock than may be observed by microscopic examination of fixed specimens. An occlusive circulatory type of shock, similar to that used previously by Allen, and more recently by Selye and Dosne, was used not only to study capillary changes but also to determine the efficacy of different methods for restoring the circulating fluid.

A comprehensive review of the literature concerning shock is unnecessary since the pertinent investigations on the subject have been presented by Cannon, Boyers, Moon, O'Shaughnessy and Slome, Blalock, and Harkins.

APPARATUS USED AND METHODS OF STUDY

A modification of the method of transillumination described by Knisely was used throughout this study and made possible the direct observation of the capillaries by means of transmitted light.§ The light source was a 400 watt bulb. The light was transmitted through a rod, which was leucite at the proximal end and silvered quartz at the distal end, and passed through an aperture measuring 2 by 3 mm. The tissue of the animal to be examined was placed over the end of the rod and direct microscopic examination of individual capillaries was made. Precautions were taken constantly against cooling or drying of the tissues. Thus, the platform on which the animal was placed was kept at body temperature, warm Ringer's solution was kept continuously flowing from the end of the rod beneath the tissues being examined, and Ringer's solution was passed over the top of the organ being examined.

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eight, twenty-two, twenty, and seventeen months, respectively. In one instance the patency recurred, apparently due to cutting through of the ligature; this recurrent patency was subsequently ligated successfully. In one instance the result is uncertain. In the two cases in which infection was present at the time of operation, no subsequent blood culture has shown organisms, and the patients are conspicuously improved six and seven months after operation.

ADDENDUM.—In the year that has elapsed since this paper was written, all of the patients reported continue in good health except for R. H. (Case 6), reported previously as having a recurrent murmur and uncertain result. This boy died in June, 1942, of complications arising from the presence of a postoperative aneurysm of the ductus. Nine other patients have been operated upon without operative mortality. Five of these, aged 1, 3, 1, 7, and 18 years, were operated upon because of systemic symptoms. All have shown benefits varying from moderate to marked. Four were operated upon because of subacute blood stream infection. One, a woman of 30 years, has been free of infection for nine months; one, a woman of 24 years, died two months after operation of bacterial endocarditis due to an associated interventricular septal defect; one, a man of 12 years, is still living six months after operation with persistent murmur and persistent subacute blood stream infection; one, a girl of 12 years is still in the postoperative period.

REFERENCES

1. Mott, Valentine: Remarks on Aneurisms, in Velpeau's Operative Surgery, WitsWood Co., 2: 306, 1851.
2. Munro, J. C.: Ligation of the Ductus Arteriosus, *Ann. Surg.* 46: 335, 1907.
3. Graybiel, A., Stueder, J. W., and Boyer, N. H.: An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient with Subacute Bacterial Endarteritis, *Am. Heart J.* 15: 621, 1938.
4. Gross, R. E., and Hubbard, J. P.: Surgical Ligation of a Patent Ductus Arteriosus; Report of First Successful Case, *J. A. M. A.* 112: 729, 1939.
5. Gross, R. E.: A Surgical Approach for Ligation of a Patent Ductus Arteriosus, *New England J. Med.* 222: 510, 1939.
6. Hubbard, J. P., Emerson, P. W., and Green, H.: Indication for the Surgical Ligation of a Patent Ductus Arteriosus, *New England J. Med.* 221: 481, 1939.
7. Gross, R. E., Emerson, P., and Green, H.: Surgical Exploration and Closure of a Patent Ductus Arteriosus, *SURGERY* 6: 201, 1939.
8. Gross, R. E.: Surgical Management of the Patent Ductus Arteriosus, *Ann. Surg.* 110: 321, 1939.
9. Bullock, L. T., Jones, J. C., and Dolley, F. S.: The Diagnosis and the Effects of Ligation of the Patent Ductus Arteriosus; A Report of Eleven Cases, *J. Pediat.* 15: 786, 1939.
10. Jones, J. C., Dolley, F. S., and Bullock, L. T.: The Diagnosis and Surgical Therapy of Patent Ductus Arteriosus, *J. Thoracic Surg.* 9: 413, 1940.
11. Burwell, C. S., Eppinger, E. C., and Gross, R. E.: The Signs of Patent Ductus Arteriosus Considered in Relation to Measurements of the Circulation, *Tr. A. Am. Physicians* 55: 71, 1940.
12. Eppinger, E. C., and Burwell, C. S.: Curable Heart Disease, *M. Clin. North America* 24: 1347, 1940.
13. Gross, R. E.: Surgical Treatment in Ten Cases of Patent Ductus Arteriosus, *J. A. M. A.* 115: 1257, 1940.
14. Eppinger, E. C., and Burwell, C. S.: The Mechanical Effects of Patent Ductus Arteriosus on the Heart, *J. A. M. A.* 115: 1262, 1940.
15. Touroff, A. S. W., and Vesell, H.: Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus, *J. A. M. A.* 115: 1270, 1940.
16. Touroff, A. S. W., and Vesell, H.: Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis with Complicating Patent Ductus Arteriosus, *J. Thoracic Surg.* 10: 59, 1940.
17. Touroff, A. S. W.: Personal Communication.
18. Gross, R. E.: Personal Communication.
19. Gross, R. E.: Surgical Closure of the Patent Ductus Arteriosus, *J. Pediat.* 17: 716, 1940.
20. Eppinger, E. C., Burwell, C. S., and Gross, R. E.: The Effects of the Patent Ductus Arteriosus on the Heart, *J. Clin. Investigation* 20: 127, 1941.
21. Miangolarra, C. J., and Gross, R. E.: Ligation of a Patent Ductus Arteriosus, *SURGERY* 9: 591, 1941.
22. Bourne, G., Keele, K. D., Tubbs, O. S., and Swain, R. H. A.: Ligation and Chemotherapy for Infection of Patent Ductus Arteriosus, *Lancet* 241: 444, 1941.

cells. Only occasionally a few small functioning capillaries (12 to 14 μ) containing a very rapid blood flow are seen among these fat cells in the normal animal. The larger capillaries (20 to 40 μ) are often seen but the circulation is so rapid within them that the individual cells cannot be delineated. The largest capillaries (150 to 250 μ), which connect the main arteriole and venule, stand out the most distinctly but the circulation within these vessels is even more rapid. The main arterioles and venules (400 to 500 μ) have such a rapid circulation that movement cannot be recognized.

Thus, as the mesentery is examined with the usual 150 magnification the main observations are indistinctness of the capillaries, the glistening white background, and the extreme rapidity of the circulation. Within the course of one to two hours, a few newly functioning capillaries appear and there is a slight slowing of the speed of the circulation. This final condition of the capillaries persists for six to seven hours and if at the end of that time the abdominal wound is repaired, the animal appears to be normal the next day.

The circulation within the liver is studied most satisfactorily with the 600 magnification water immersion system. With this magnification the appearance of the sinusoids (40 to 50 μ) is variable not only in their content but also in the speed of the blood flowing through them. When first examined, many of the hepatic sinusoids are empty, a few contain cells but are inactive, and others reveal such a rapid circulation that the individual cells cannot be recognized. The circulation within the larger vessels is extremely rapid. Gradually during the following eight hours, there is a slowing of the sinusoidal circulation, making it possible to observe individual cells in the rapidly moving current. It is unusual for an alteration of the circulation in the large vessels to occur. At the end of this eight-hour period, there are fewer sinusoids in the inactive phase and all the sinusoids are more congested than at the beginning of the examination but there is no sluggishness of circulation or generalized stasis.

2. Effect After Administration of Histamine

There was no change in the appearance of the capillaries of the mesentery or liver following the local application of a 1 per cent solution of histamine.

Variable effects, depending on the dose, were observed after intravenous administration of histamine. Any effect after intravenous administration of 1 to 6 mg. of histamine was rarely noted. However, there was observed the appearance of newly functioning capillaries in the mesentery with some slowing of the flow of blood with doses of 6 to 12 mg. of the histamine base. Nothing definite was noted in the liver with such doses. Very definite results occurred when 12 to 20 mg. of the base per 100 Gm. of body weight was given. Many newly functioning capillaries appeared, the larger capillaries stood out more distinctly, there was a definite slowing of the circulation, and congestion and

Six-week-old albino male rats of the Wistar strain, ranging from 70 to 140 Gm. were used. Pentobarbital sodium (nembutal) was used throughout as an anesthetic agent in subcutaneous doses of 30 mg. per kilogram. As necessary, 1 to 1.5 mg. more was given. No effect on the capillaries from such doses was ever noted.

The normal circulation of the mesentery and liver was studied first. A routine of using one area of the mesentery only once for observation was adopted. Observations were made first on the mesenteric field at the ileocecal junction and further observations during the course of the experiment were made on successive fields passing proximally. As far as was possible, a similar routine was adopted for study of the borders of the liver, beginning at the far left border and observing successive fields to the right. These various fields were studied with the binocular stageless microscope using 40, 150, and, by use of a water immersion lens system, 600 magnifications.

The effects of local and intravenous administration of histamine were observed on both the mesenteric and hepatic circulation.

A condition simulating shock was not produced by simple laparotomy, exposure of the intestines, or crushing trauma to the limbs. A shock-like condition was produced by any of the following three methods:

1. *Intestinal manipulation:* The intestines were manipulated firmly but gently, so that no gross hemorrhage occurred. The manipulation was continuous for five minutes. The intestines then were left exposed on the warm platform for the remainder of the period of observation.

2. *Exposure of intestines to cold:* The animal was placed on a glass plate, which in turn was placed on a piece of ice. The intestines were removed from the abdominal cavity and spread over the glass plate.

3. *Application of rubber bands to thighs:* The animals were given pentobarbital sodium and rubber bands were tied tightly, high on the legs. The animals then were left alone for five to five and one-half hours. At this time the animals were again given pentobarbital sodium and the abdomen was opened. After observations of the capillaries of mesentery and liver had been made, the rubber bands were cut.

In all types of shock, observations of respiration and of mesenteric and hepatic capillaries were made and recorded every fifteen to thirty minutes. After the findings in these different types of shock had been confirmed on numerous occasions, further studies were made in an attempt to correlate the state of shock with the concentration of blood. Erythrocyte counts and hematocrit readings (Van Allen method) were made on the blood secured by means of cardiac puncture three days to one week before shock was induced experimentally. Specimens of blood were obtained again just before death in the condition of shock.

RESULTS

1. *The Normal Animal*

Observation of the mesenteric circulation reveals, with all magnifications, a glistening white background which is composed of the fat

change was due to the appearance of newly functioning capillaries which were congested and stasis rapidly developed. Dilatation and congestion occurred in the larger capillaries and the circulation became sluggish. Groups of red blood cells appeared in many fields outside of the capillaries in thirty minutes to one hour.

(2) *Liver*: All the sinusoids became active; however, the circulation was sluggish within fifteen to thirty minutes after the intestines had been manipulated and gradual stasis took place. Even though there was increased sinusoidal activity, congestion was not as marked as is often seen in the normal liver.

After the capillary response in this type of shock was established, hematocrit and red blood cell studies were done and often the values were found to be quite variable. The respirations remained at 80 to 90 a minute; however, a few minutes prior to death they would gradually decrease, become gasping, and finally cease.

b. Exposure of Intestines on Iced Plate (Table 2).—

(1) *Mesentery*: The circulation usually remained very rapid throughout this type of shock, even though the respiration would cease temporarily for ten to fifteen minutes. A few newly functioning capillaries appeared but stasis did not occur until shortly before the death of the animal and dilatation with congestion usually was not seen.

TABLE II
EFFECT OF EXPOSURE OF INTESTINE ON ICED PLATE

NUM- BER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
EXPOSURE					
1	87.2	1°40'	-0.52	-5	Mesentery: Even though respirations stopped for 10 to 15 minutes, circula- tion remained very rapid; new capillaries appeared but stasis was terminal Liver: Sinusoids active and con- gested; often seen were groups of red blood cells outside the sinusoids
2	96.0	1°40'	0.50	3	
3	98.0	1°45'	1.42	17	
4	66.2	48'	-0.25	-8	
CONTROLS					
1	104.4	1°40'+	-0.59	-6	Mesentery and liver: As in normal control in Table I
2	102.8	2° +	0.37	-1	

*Millions per c. mm. of blood.

(2) *Liver*: The sinusoids became very active and congested and groups of red blood cells often were seen outside of the sinusoids. Gradual slowing took place thirty to forty-five minutes prior to death and stasis finally occurred. More congestion of the sinusoids was seen in this type of shock than in any other type.

The animal was placed on a glass plate over ice with the intestines spread out on the plate. The respirations would decrease and become

dilatation occurred. The sinusoids of the liver were congested and the flow of blood was slowed in both the sinusoids and larger vessels. The mesenteric circulation gradually returned to normal within ten to fifteen minutes, the hepatic circulation returning to normal in ten to thirty minutes. The lethal dose was found to be 27 to 33 mg. of histamine base for a rat weighing 100 Gm.

The main feature accompanying the capillary change was a marked decrease in respiration, from a range of 80 to 100 to a range of 60 to 70 respirations a minute. Also coinciding with the return of the capillaries to normal, the respirations would become normal again within ten to fifteen minutes after the intravenous injection of histamine.

When the lethal doses were administered the respirations decreased quickly, the capillary changes were minimal, and often no difference was observed from the normal except for the cessation of flow of blood.

Lacrimation; profuse, watery mucoid discharge from the nose and mouth; restlessness; increased peristalsis; occasional convulsive seizures of the limbs, and also, on occasions, micturition and defecation occurred with doses of 8 to 20 mg. of histamine administered intravenously.

3. Experiments Dealing With Shock

a. Intestinal Manipulation (Table I).—(1) Mesentery: A pink background developed, replacing the normal glistening white background within fifteen to thirty minutes after the intestinal manipulation. This

TABLE I
EFFECT OF INTESTINAL MANIPULATION FOR FIVE MINUTES

NUMBER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATOCRIT (PER CENT)	
MANIPULATION					
1	101.5	1°40'	3.31	19	Mesentery: A pink background developed within 15 to 30 minutes, and within 30 to 60 minutes hemorrhages appeared in many fields Liver: Sluggish circulation developed in all the sinusoids within 15 to 30 minutes with gradual stasis occurring
2	105.0	25'	0.74	5	
3	99.8	2°19'	1.81	8	
4	82.4	21'	0.30	6	
5	82.8	46'	2.29	19	
CONTROLS					
1	57.2	2°30'+	0.04	1	Mesentery: Capillaries not clearly delineated, white background, rapid circulation; after 30 to 60 minutes, new small capillaries appeared, but circulation remained rapid Liver: More sinusoids gradually resumed activity but circulation remained very rapid throughout
2	86.8	1°20'+	-0.64	0	

*Millions per c. mm. of blood.

TABLE III

EFFECT OF RUBBER BANDS ON THIGHS FOR FIVE TO FIVE AND ONE-HALF HOURS

NUM- BER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
RUBBER BANDS ON THIGHS					
1†	76.5	0	0.32	-2	Mesentery: Entirely normal for first 30 to 60 minutes after bands had been cut; then new capillaries appeared, main capillaries stood out more clearly, circulation slowed and became sluggish as capillaries became dilated, congested and finally static Liver: Remained normal for 30 to 90 minutes, then gradually the circulation became sluggish and stasis occurred first in sinusoids, then in larger veins; often not as much congestion as normal
2	101.6	2°46'	1.73	16	
3	104.5	3°9'	3.33	19	
4	110.5	2°40'	2.64	21	
5	67.0	1°53'	1.73	19	
6	78.4	1°12'	3.34	34	
7	100.5	1°37'	4.76	40	
8	107.7	1°45'	3.54	28	
CONTROLS					
1	94.0	2°37'	0.45	-7	Mesentery and liver: As in normal control in Table I
2	85.4	1°55'+	-0.78	-8	
3	101.0	2°5'+	1.10	-1	

*Millions per c. mm. of blood.

†Died from effect of pentobarbital sodium before bands were cut.

became active but often they were not as congested as they are normally. The circulation became sluggish and finally stasis occurred, first in the sinusoids and then in the larger veins.

Edema rapidly accumulated in the legs of the animals after the bands were cut, being so marked that the legs became abducted and externally rotated. The average increase of the circumference at the tibial tubercle from the time that the bands were cut until the respirations had ceased was 0.7 to 0.8 cm.

4. Studies in Regard to Causation of the Rubber Band Type of Shock

a. *Wrapping of the Legs* (Table IV, Fig. 1, b).—The legs of the animals were wrapped tightly with waterproof adhesive tape just before the bands were cut. These wrappings were reinforced further with tape after the bands were cut.

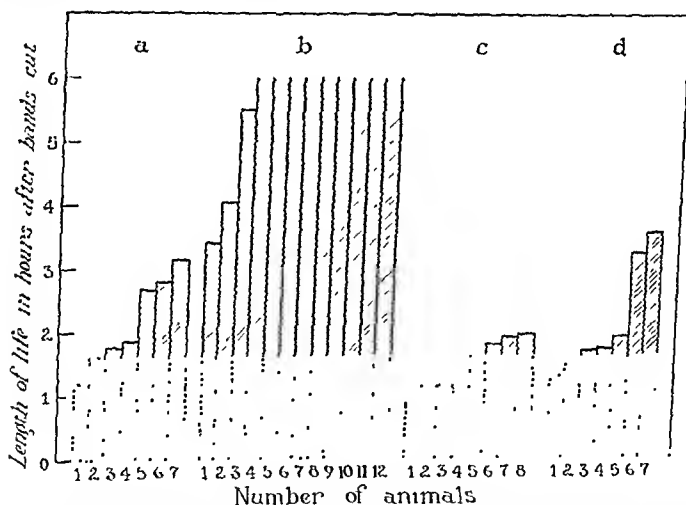
(1) *Mesentery and Liver*: The usual capillary response was that of the normal control animal. Unless the legs were wrapped tightly, some edema did develop under the tape and the usual capillary response to shock was present, hemoconcentration occurred, and the animals died.

The controls in this series were divided into two groups. Group *a* consisted of animals whose legs were wrapped tightly with tape at the same time the other animals' legs were wrapped, but no rubber bands had been applied previously.

Group *b* consisted of animals whose legs were wrapped tightly with tape for five hours and then the tape was removed.

irregular within eight to twelve minutes, and ten to twenty minutes later the respirations would cease entirely. The animals were left in such a condition as long as twenty minutes without being disturbed. Finally when they were examined, the foregoing capillary changes were observed. The rats then were placed on the warm platform. After the animals had been on the warm platform for two to three minutes, the respirations gradually began to increase but did not return to the normal rate. This sequence of events would repeat itself; each time that the rat was placed on the warm platform the respiratory rate would increase but each time the maximal respiratory rate was less than on the previous occasion. Finally, the respirations ceased entirely even when the animal was kept on the warm platform.

There was no consistency in the results of hematocrit and red blood cell studies in this type of shock.



Figs. 1 to 4 show the same relationship, that is, the ordinate is equal to the number of hours that the animal lived after the rubber bands were cut and the abscissa represents the number of animals used in each series.

Fig. 1.—Study of the causation of the rubber band type of shock. a, The usual rubber band type of shock; b, the legs of the animals were wrapped tightly before the bands were cut; c, the wrappings were removed from the legs one hour after the bands were cut; d, spinal cords resected before the bands were cut.

c. Application of Rubber Bands to Thighs (Table III, Fig. 1, a).—

(1) *Mesentery*: There was no change from the normal capillary circulation either before the bands were cut or for thirty to sixty minutes after the cutting of the bands. At this time, newly functioning capillaries appeared and there was a slowing of the speed of the circulation. The larger capillaries stood out more distinctly than before and dilatation occurred. Gradually the circulation became sluggish and stasis resulted shortly before the death of the animal.

(2) *Liver*: The circulation remained normal for thirty to ninety minutes after the rubber bands were cut. All the sinusoids gradually

TABLE III

EFFECT OF RUBBER BANDS ON THIGHS FOR FIVE TO FIVE AND ONE-HALF HOURS

NUMBER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
RUBBER BANDS ON THIGHS					
1†	76.5	0	0.32	-2	Mesentery: Entirely normal for first 30 to 60 minutes after bands had been cut; then new capillaries appeared, main capillaries stood out more clearly, circulation slowed and became sluggish as capillaries became dilated, congested and finally static Liver: Remained normal for 30 to 90 minutes, then gradually the circulation became sluggish and stasis occurred first in sinusoids, then in larger veins; often not as much congestion as normal
2	101.6	2°46'	1.73	16	
3	104.5	3°9'	3.33	19	
4	110.5	2°40'	2.64	21	
5	67.0	1°53'	1.73	19	
6	78.4	1°12'	3.34	34	
7	100.5	1°37'	4.76	40	
8	107.7	1°45'	3.54	28	
CONTROLS					
1	94.0	2°37'	0.45	-7	Mesentery and liver: As in normal control in Table I
2	85.4	1°55'+	-0.78	-8	
3	101.0	2°5'+	1.10	-1	

*Millions per c. mm. of blood.

†Died from effect of pentobarbital sodium before bands were cut.

became active but often they were not as congested as they are normally. The circulation became sluggish and finally stasis occurred, first in the sinusoids and then in the larger veins.

Edema rapidly accumulated in the legs of the animals after the bands were cut, being so marked that the legs became abducted and externally rotated. The average increase of the circumference at the tibial tubercle from the time that the bands were cut until the respirations had ceased was 0.7 to 0.8 cm.

4. Studies in Regard to Causation of the Rubber Band Type of Shock

a. *Wrapping of the Legs* (Table IV, Fig. 1, b).—The legs of the animals were wrapped tightly with waterproof adhesive tape just before the bands were cut. These wrappings were reinforced further with tape after the bands were cut.

(1) *Mesentery and Liver*: The usual capillary response was that of the normal control animal. Unless the legs were wrapped tightly, some edema did develop under the tape and the usual capillary response to shock was present, hemoconcentration occurred, and the animals died.

The controls in this series were divided into two groups. Group a consisted of animals whose legs were wrapped tightly with tape at the same time the other animals' legs were wrapped, but no rubber bands had been applied previously.

Group b consisted of animals whose legs were wrapped tightly with tape for five hours and then the tape was removed.

TABLE IV
EFFECT OF RUBBER BANDS ON THIGHS AND WRAPPING OF LEGS WHEN BANDS WERE CUT

NUM- BER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
LEGS WRAPPED TIGHTLY					
1	93.4	4°2'	0.82	4	Mesentery: Usually the normal capillary circulation was seen throughout the entire six-hour period Liver: Not different from normal, sinusoids remaining very active throughout Note: Only abnormal feature seen in this group was the edema of the scrotum and penis, with occasional urethral discharge. This edema was very marked in Animal 6 and the scrotum became enormous and blue; this was the only animal in the group which had the usual capillary changes seen in shock (see Table III)
2	91.0	6°+	0.27	4	
3	106.0	6°+	0.52	1	
4	104.0	6°+	0.05	-3	
5	118.4	6°+	0.48	1	
6	121.1	3°25'	0.82	17	
7	124.8	6°+	0.87	3	
8	87.0	5°29'	0.30	8	
9	112.5	6°+	0.07	-2	
10	106.0	6°+	0.44	6	
11	130.6	6°+	0.06	-2	
12	126.4	6°+	0.14	1	
LEGS WRAPPED LOOSELY					
1	106.0	3°9'	1.21	25	Mesentery and liver: Capillary changes as seen in Table III
2	100.2	2°50'	0.43	14	
CONTROLS A: ONLY LEGS WRAPPED; RUBBER BANDS NOT APPLIED					
1	89.2	2°46'	0.49	8	Mesentery and liver: Entirely normal (Table I)
2	104.1	3°12'+	0.27	4	
3	92.4	6°+	-0.80	-4	
4	137.2	6°+	0.54	8	
CONTROLS B: LEGS WRAPPED THEN TAPE REMOVED					
1	128.2	6°+	0.35	3	Mesentery and liver: See normal control in Table I; even though these legs were wrapped very tightly, the tourniquet effect of the rubber band was not present
2	126.4	6°+	0.30	-4	
3	128.6	6°+	0.07	-1	

*Millions per c. mm. of blood.

An experiment then was done to observe the effects of temporary splinting of the legs (Table V, Fig. 1 c). The rubber bands were placed around the hind legs for the usual five-hour period, the legs were wrapped tightly with adhesive tape, and the bands were cut. At the end of one hour the adhesive tape wrappings were removed. The legs began to swell rapidly and within thirty minutes the usual capillary response seen in the rubber band type of shock developed. Hemococoncentration was present and there was the usual increase of the size of the legs. The controls in this group were animals on whose legs the rubber bands were left throughout the entire experiment and all of these animals lived for the six-hour period of observation. The capillary response was that of the normal animal; there was no increase of the size of the legs and hemococoncentration did not develop.

TABLE V

EFFECT OF REMOVING WRAPPING OF LEGS AN HOUR AFTER RUBBER BANDS WERE CUT

NUMBER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
LEGS WRAPPED TIGHTLY WHEN BANDS WERE CUT; TAPES OFF AFTER 1 HOUR					
1	123.4	53'	1.92	21	Mesentery: Entirely normal until 15 to 30 minutes after removal of wrappings, then the usual change of appearance of new capillaries, slowing circulation, increasing congestion, sluggishness, dilation, and terminal stasis was seen Liver: No change from normal until after removal of wrappings; then gradual slowing of the circulation in the sinusoids with stasis and finally stasis in the larger veins of the liver were seen
2	127.2	1°37'	1.98	23	
3	124.2	1°8'	2.07	29	
4	168.2	1°9'	2.37	36	
5	163.2	1°28'	2.40	25	
6	155.4	1°48'	2.45	30	
7	139.2	1°57'	1.06	19	
8	110.0	1°54'	2.96	28	
CONTROLS: BANDS LEFT ON					
1	102.6	6°+	0.26	- 3	Mesentery and liver: No difference from the normal control animals of Table I
2	103.4	6°+	0.15	6	
3	125.2	6°+	-0.45	-10	
4	140.4	6°+	-0.99	0	

*Millions per c. mm. of blood.

The question then arose: When the legs are wrapped tightly with adhesive tape, is not the same tourniquet effect present as though the rubber bands were left on throughout the experiment? The adhesive wrappings were proved not to have such an effect by the following observations:

1. When the bands were cut, even though the legs were wrapped tightly, there was a return of the feet to a more normal color.
2. Small cuts and bites on the feet would bleed when the bands were cut, even though the legs were wrapped tightly.

3. Shock could not be produced (control Group *b*, Table IV) by wrapping the legs tightly for five hours and then removing the wrappings.

In order to determine whether the rubber band type of trauma was caused by bombardment of sensory impulses from the traumatized region, the lumbar portions of the spinal cords of eight rats were sectioned. The length of life of seven of the rats after the rubber bands were cut is given in Fig. 1, *d*. Further details are presented in later paragraphs.

In order to check further the effect of preventing loss of fluid by wrapping the legs, two dozen animals were divided into four groups.

Group *a* was composed of six animals with rubber bands placed around all four legs for more than four hours. The bands then were cut. No animal lived longer than two hours and thirty-two minutes (Fig. 2, *a*).

Group *b* was composed of the same number of animals and the same method was used, except that all four legs of the animals were wrapped

TABLE IV
EFFECT OF RUBBER BANDS ON THIGHS AND WRAPPING OF LEGS WHEN BANDS
WERE CUT

NUM- BER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			LFD BLOOD CELLS*	HFMATO CRIT (PFR CENT)	
LEGS WRAPPED TIGHTLY					
1	93.1	1°2'	0.82	4	Mesentery: Usually the normal capillary circulation was seen throughout the entire six hour period Liver: Not different from normal, sinusoids remaining very active throughout Note: Only abnormal feature seen in this group was the edema of the scrotum and penis, with occasional urethral discharge. This edema was very marked in Animal 6 and the scrotum became enormous and blue; this was the only animal in the group which had the usual capillary changes seen in shock (see Table III)
2	94.0	6°+	0.27	4	
3	106.0	6°+	0.52	1	
4	104.0	6°+	0.05	-3	
5	118.4	6°+	0.48	1	
6	121.1	3°25'	0.82	17	
7	121.8	6°+	0.87	3	
8	87.0	5°29'	0.30	8	
9	112.5	6°+	0.07	-2	
10	106.0	6°+	0.44	6	
11	130.6	6°+	0.06	-2	
12	126.4	6°+	0.14	1	
LEGS WRAPPED LOOSELY					
1	106.0	3°9'	1.21	25	Mesentery and liver: Capillary changes as seen in Table III
2	100.2	2°50'	0.43	14	
CONTROLS A. ONLY LEGS WRAPPED; RUBBER BANDS NOT APPLIED					
1	89.2	2°46'	0.49	8	Mesentery and liver: Entirely normal (Table I)
2	104.1	3°12'+	0.27	4	
3	92.4	6°+	-0.80	-4	
4	137.2	6°+	0.54	8	
CONTROLS B: LEGS WRAPPED THEN TAPE REMOVED					
1	128.2	6°+	0.35	3	Mesentery and liver: See normal control in Table I; even though these legs were wrapped very tightly, the tourniquet effect of the rubber band was not present
2	126.4	6°+	0.30	-4	
3	128.6	6°+	0.07	-1	

*Millions per c mm of blood

An experiment then was done to observe the effects of temporary splinting of the legs (Table V, Fig. 1 c). The rubber bands were placed around the hind legs for the usual five-hour period, the legs were wrapped tightly with adhesive tape, and the bands were cut. At the end of one hour the adhesive tape wrappings were removed. The legs began to swell rapidly and within thirty minutes the usual capillary response seen in the rubber band type of shock developed. Hemoconcentration was present and there was the usual increase of the size of the legs. The controls in this group were animals on whose legs the rubber bands were left throughout the entire experiment and all of these animals lived for the six-hour period of observation. The capillary response was that of the normal animal; there was no increase of the size of the legs and hemoconcentration did not develop.

Rubber bands were applied to the hind legs of Group *d* and the legs were wrapped tightly with adhesive tape before the bands were cut. All six of these animals lived throughout the six-hour period of observation, five lived for twenty-four hours and three were living at the end of five days (Fig. 2, *d*).

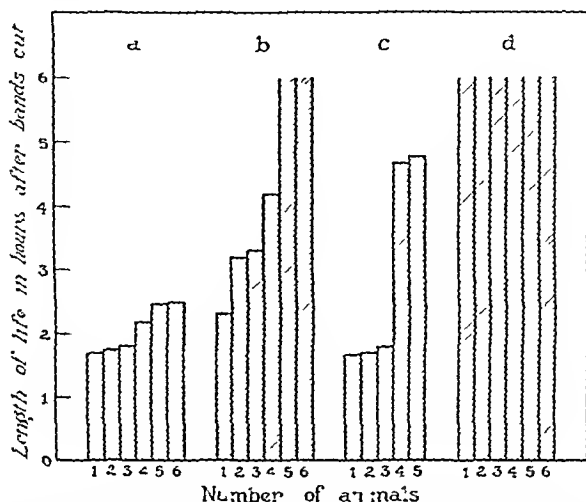


Fig. 2.—Further study, showing the importance of local loss of fluid. *a*, Bands placed around all four legs and then cut. *b*, bands placed around all four legs, then legs wrapped tightly before the bands were cut; *c*, bands placed around hind legs and then cut, *d*, hind legs wrapped tightly before bands were cut.

b. Section of the Spinal Cord (Table VI, Fig. 1, *d*).—The lumbar portion of the spinal cord was sectioned and the distal segment of the cord was needled. In some of the animals, $1\frac{5}{100}$ c.c. of 10 per cent procaine hydrochloride was injected into the distal segments of the spinal cords.

(1) *Mesentery*: Animals whose spinal cords had been sectioned either just before or just after the rubber bands were cut revealed the usual changes seen in the rubber band type of shock. However, in the other animals in this group, whose spinal cords had been sectioned two to four days before the rubber bands were applied, there were innumerable newly functioning capillaries. Congestion and dilatation were generalized and the circulation was much slower than normal. The only noticeable change after the bands were cut was a gradual slowing of the circulation, occurring forty-five minutes or later with terminal stasis. Cord bladders were also very prominent in this latter group.

5. Intravenous Therapy With the Rubber Band Type of Shock

a. Ringer's Solution (Table VII).—Ringer's solution, 3 c.c. was given intravenously into the inferior vena cava over the course of one minute at the time the rubber bands were cut.

SURGERY

TABLE VI

EFFECT OF SECTION OF THE SPINAL CORD ON RATS WHOSE LEGS WERE CONSTRICTED WITH RUBBER BANDS

TIME CORDS CUT	NUM- BER	WEIGHT (G.M.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
				RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
When bands were cut	1 2	138.0 99.4	1°18' 1°41'	3.25 3.03	25 24	Mesentery and liver: First four animals as described in Table III, the typical gradual onset of capillary stasis
Five hours before bands were cut	3 4	129.2 104.6	1°44'	-0.61 1.99	- 2 23	
Two days before bands were applied	5 6	113.0 127.6	1°33' 3°34'	1.69 3.01	17 21	
Four days before bands were applied	7 8	144.8 144.6	1°57' 3°17'	2.63 2.39	18 24	

However, in Animals 5 and 6 and to a greater degree in Animals 7 and 8 there were multiple new capillaries in the mesenteric field on first examination with slower circulation than normal; this was not seen in the hepatic sinusoids

CONTROLS						Mesentery and liver: Same as normal with exception of Animal 3 which revealed the multiple new capillaries in the mesentery and no change after 4 hours
When bands were cut	1	134.8	3°+	0.70	5	
Five hours before bands cut	2	141.6	2°+	0.55	1	
Two days before bands ap- plied	3	140.0	4°+	0.02	- 5	

*Millions per c. mm. of blood.

TABLE VII

EFFECT OF INTRAVENOUS INJECTION OF RINGER'S SOLUTION WHEN RUBBER BANDS WERE CUT

NUM- BER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATO- CRIT (PER CENT)	
1	129.4	3°16'	1.35	17	Mesentery: Following intravenous injection many new capillaries became apparent, with slight slowing of circulation; one hour later, usual changes seen in shock developed. Liver: Not different from the capillary effects described in Table III.
2	92.0	2°33'	2.55	30	
3	130.5	3°9'	1.57	18	

*Millions per c. mm. of blood.

tightly with adhesive tape just before the bands were cut. Two of these animals lived for six hours but were dead at the end of twenty-four hours (Fig. 2, b).

Rubber bands were applied to the hind legs of Group c for five and one-half hours and then cut. The longest period of life was four hours and forty-seven minutes (Fig. 2, c).

TABLE VIII

EFFECT OF INTRAVENOUS INJECTION OF WHOLE BLOOD WHEN RUBBER BANDS WERE CUT

NUMBER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATOCRIT (PER CENT)	
1	97.5	3°2'	4.99	30	Mesentery: Following intravenous injection, many new capillaries appeared, with congestion and slowed circulation. The capillaries of Animal 7 remained this way; the other animals gradually went into shock, however, capillary stasis was present 1 to 2 hours before death rather than being a terminal phenomenon. Liver: Sinusoids were very full and distended, after intravenous injection and stasis occurred 45 minutes to 1½ hour before death
2	122.2	3°47'	3.62	21	
3	120.6	4°17'	3.46	29	
4	109.7	4°26'	4.92	36	
5	127.2	4°12'	3.91	29	
6	116.0	3°27'	3.64	31	
7	130.6	6°+	0.71	16	
8	112.5	3°23'	3.07	37	
9	130.4	3°7'	2.03	19	

*Millions per c. mm. of blood.

(2) *Liver*: Increased activity of the sinusoids was present following the blood transfusion. The sinusoids became widely dilated and marked congestion was present. Absolute stasis occurred forty-five minutes to one and one-half hour prior to the cessation of respirations.

The length of life of the animals in this series was prolonged definitely (Fig. 3, c) and two to four additional doses of pentobarbital sodium were needed during the course of the experiments. Even when complete stasis was present, the animal was restless and needed more anesthetic. The respiratory rate went as high as 160 to 240 a minute and remained elevated for one to two hours before the respirations ceased. One animal lived for the six-hour period of observation without exhibiting any capillary stasis and the hemoconcentration in this animal was not as marked as in the remainder of the group.

The legs were much more edematous than usual, the circumference at the tibial tubercle showing an increase of 1.4 to 1.8 cm. rather than the increase of 0.7 to 0.8 cm. seen in the usual untreated type of rubber band trauma.

c. *Blood plasma* (Table IX).—Blood plasma was first made by mixing 8 to 12 c.c. of blood with 0.5 to 1.0 c.c. of 10 per cent solution of heparin. The blood then was centrifuged for twenty minutes and the supernatant plasma was removed. Blood plasma, 3 to 3.5 c.c., was given intravenously at the time the rubber bands were cut. Considerable hemorrhage was encountered on some occasions so that subsequently a 5 per cent solution of heparin was used in this procedure with better success.

(1) *Mesentery*: The capillary response resembled that found after intravenous administration of Ringer's solution. Immediately following the injection of plasma, a few newly functioning capillaries appeared

(1) *Mesentery*: Following the intravenous injection, newly functioning capillaries appeared and the circulation was slower than normal, but no obvious dilatation or congestion was present. About one and one-half hour later, the circulation became much slower and dilatation and congestion occurred with terminal stasis.

(2) *Liver*: Following the injection, all of the sinusoids became active but not congested. After one and one-half hour, the circulation gradually slowed down and terminal stasis occurred.

On comparison of untreated rats to the thighs of which rubber bands had been applied (Fig. 3, *a*) with the rats that had received Ringer's solution (Fig. 3, *b*), it was evident that life was prolonged to some

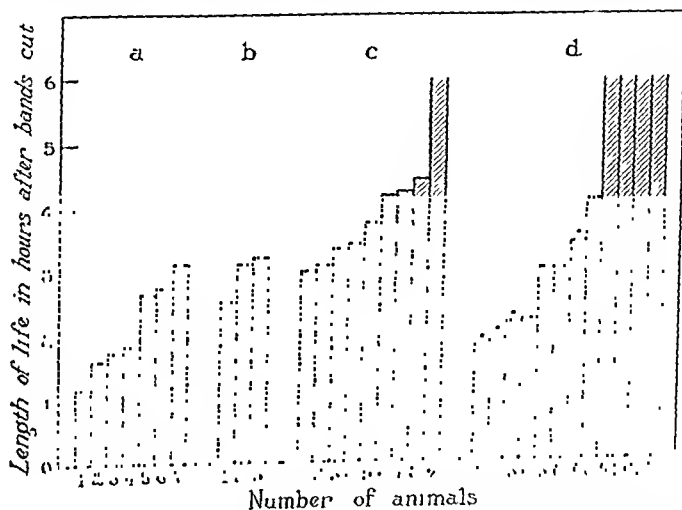


Fig. 3.—Effects of intravenous therapy. *a*, Usual rubber band type of shock in untreated rats; *b*, Ringer's solution given intravenously before bands were cut; *c*, whole blood given intravenously before bands were cut; *d*, blood plasma given intravenously before bands were cut.

*Denotes that hemorrhage occurred.

extent in the latter group and it was necessary to give an additional dose of pentobarbital sodium to each animal in this series; whereas, with the usual untreated type of rubber band trauma, none but the initial dose of pentobarbital sodium was needed.

The legs were much more edematous than in the ordinary type of rubber band trauma and hemoconcentration was present.

b. Whole Blood (Table VIII).—Rat's whole blood, 15 c.c., was mixed with 2 c.c. of a 2.5 per cent solution of sodium citrate. This mixture was filtered through gauze and 3 to 4 c.c. was given intravenously at the time the rubber bands were cut.

(1) *Mesentery*: Many newly functioning capillaries appeared and marked congestion developed with slowing of the circulation. In all cases, stasis occurred about one to two hours before the respirations ceased.

death was seen with terminal stasis in those animals that died, whereas in those that lived the sinusoidal circulation remained quite rapid.

In the cases of hemorrhage, although congestion did not develop, the paleness seen in the mesentery was not present.

The lives of four of these animals (a third of the group) persisted for the six-hour period of observation and those that died needed two to four additional doses of pentobarbital sodium (Fig. 3, *d*). The abdomen of one animal was closed after the specimens for hematoerit and cell counts were taken by cardiac puncture through the diaphragm and this animal was living at the end of two days with increasing edema.

There was the usual increase of the size of the legs of this group as observed in all the animals treated with intravenous fluids.

There was no difference in the respirations of the untreated group, those treated with Ringer's solution, or those treated with blood plasma.

6. Adrenal Cortical Hormone With Rubber Band Type of Shock

This is illustrated in Fig. 4. Thirty-six animals were divided into four groups of nine animals each.

The animals in Group *a* received 1 c.c. of Ringer's solution subcutaneously on three consecutive days, while those in Group *b* received 1 c.c. of adrenal cortical extract mixture (667-1 Kendall's laboratories), in which each cubic centimeter was equal to 75 Gm. of the gland, subcutaneously on three consecutive days. The last dose in all cases of Groups *a* and *b* was given one hour before the rubber bands were cut on the third day. One animal in Group *b* died from the effects of administration of pentobarbital sodium at the time of application of the rubber bands.

There was a suggestive increase of the length of life of the animals in Group *b* over those in Group *a*, but certainly nothing conclusive (Fig. 4, *a* and *b*).

The animals in Group *c* were given 2 c.c. of sesame oil subcutaneously two and one-half hours after the bands were applied and those in Group *d* were given 2 c.c. of adrenal cortical extract in sesame oil subcutaneously at the same time. (Two cubic centimeters of this mixture was equal to 1 mg. of compound E and equal also to 1,500 Gm. of the gland.) The bands were left on for a total of five hours.

There was no demonstrable difference between the two groups in respect to length of life after the bands were cut (Fig. 4, *c* and *d*).

SUMMARY AND CONCLUSIONS

1. A comparison of the effects of histamine and shock on the capillary bed with the normal capillary circulation has been presented.

2. Histamine, when applied locally to the mesentery and liver of the rat, had no demonstrable effect on the capillaries. Very definite capillary effects were observed when histamine was given in large doses (12 to 20 mg. of the base per 100 Gm. of body weight) by the intra-

TABLE IX

EFFECT OF INTRAVENOUS INJECTION OF BLOOD PLASMA WHEN RUBBER BANDS WERE CUT

NUMBER	WEIGHT (GM.)	DURATION OF LIFE	DIFFERENCE IN		CAPILLARY RESPONSE
			RED BLOOD CELLS*	HEMATOCRIT (PER CENT)	
1	134.6	6°+	0.52	13	Mesentery: Not different from the group treated with Ringer's solution except in Animals 1, 2, 8, and 12 which lived for 6 hours, and their capillary circulation returned to normal
2	126.5	6°+	0.29	9	
3	116.5	2°14'	2.20	32	
4†	152.6	2°12'	0.21	13	
5†	109.5	1°58'	-0.56	0	
6	118.2	3°3'	2.51	21	Liver: As in Table III, except those animals that lived, in which the sinusoidal circulation remained very active
7†	101.4	3°27'	0.33	11	
8	144.5	6°+	0.83	11	
9†	128.5	1°53'	1.81	25	
10	122.5	4°8'	1.42	13	
11	111.0	3°3'	1.74	17	
12	120.4	6°+	0.53	14	

*Millions per c. mm. of blood.

†Denotes hemorrhage.

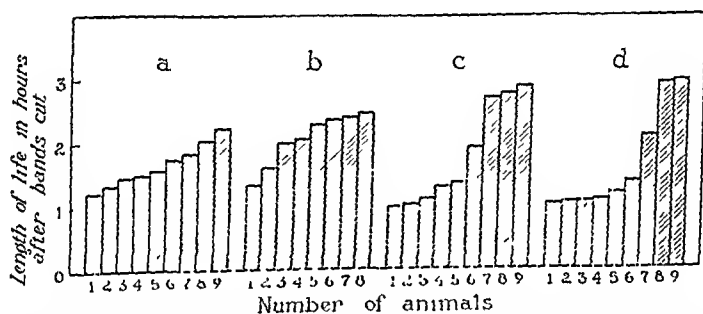


Fig. 4.—Effects of adrenal cortical hormone alone. *a*, Animals given 1 c.c. of Ringer's solution subcutaneously on three consecutive days, then shock induced; *b*, animals given 1 c.c. of adrenal cortical mixture in Ringer's solution subcutaneously on three consecutive days, then shock induced (each cubic centimeter of adrenal cortical mixture equals 75 Gm. of the gland); *c*, treated with 2 c.c. of sesame oil subcutaneously two and one-half hours before shock was induced; *d*, treated with 2 c.c. of adrenal cortical extract in sesame oil two and one-half hours before shock was induced. (Such a dose was equal to 1 mg. of compound E and 1,500 Gm. of the gland.)

and a slight slowing of the circulation often was seen. In a few instances, this effect was temporary and the circulation soon became normal. In the others the decreased circulatory speed was maintained and one to two hours prior to death the circulation became sluggish but stasis was a terminal phenomenon rather than an early occurrence as seen with the use of whole blood.

In those animals in which hemorrhage occurred, dilatation was present, but few cells were present in the terminal stages, resulting in a vacant appearance of the capillaries and a pale appearance of the region in general.

(2) *Liver*: All of the sinusoids became very active, maintaining a rapid circulation, but were not markedly congested. The usual response of slowing of the circulation one hour to one hour and a half prior to

of observation. Accompanying the prolonged period of capillary stasis was the persistence of a very rapid respiratory rate for about one hour prior to the death of the animals.

c. Blood plasma allowed the animals to live longer than the controls, one third of the animals living for the six-hour period of observation. This fluid was definitely the most efficacious in preventing the onset of shock.

6. Adrenal cortical hormone, used alone, was of no effect in prolonging the lives of the animals undergoing the rubber band type of trauma.

REFERENCES

1. Allen, F. M.: Physical and Toxic Factors in Shock, *Arch. Surg.* 38: 155-180, 1939.
2. Blalock, Alfred: Principles of Surgical Care; Shock and Other Problems, St. Louis, 1940, C. V. Mosby Company, pp. 91-187.
3. Boyers, L. M.: Shock; Study of Partial Available Modern Literature of Shock, *Am. J. Surg.* 36: 623-652, 1937.
4. Cannon, W. B.: Traumatic Shock, New York, 1923, D. Appleton and Company, 201 pp.
5. Harkins, H. N.: Recent Advances in the Study and Management of Traumatic Shock, *SURGERY* 9: 231-294; 446-482; 607-655, 1941.
6. Knisely, M. H.: An Improved Fused Quartz Living Tissue Illuminator, *Anat. Rec.* 71: 503-507, 1938.
7. Moon, V. H.: Shock and Related Capillary Phenomena, New York, 1938, Oxford University Press, 442 pp.
8. O'Shaughnessy, Laurence, and Slome, David: Etiology of Traumatic Shock, *Brit. J. Surg.* 22: 589-618, 1935.
9. Selye, Hans, and Dosne, Cristiane: Changes in Chemical Composition of the Blood Coming From Damaged Tissues, *Proc. Soc. Exper. Biol. & Med.* 47: 143-148, 1941.
10. Wakim, K. G.: Studies on the Intrahepatic Circulation in the Intact Animal, Thesis, Graduate School of the University of Minnesota, 1941.

venous route. When given rapidly into the veins, 27 to 33 mg. of the base per 100 Gm. of body weight was found to be the lethal dose.

3. In the rat, shock was produced by intestinal manipulation, exposure of intestines to cold, and occlusion of the circulation to the hind limbs by means of rubber bands.

4. The causation of the rubber band type of trauma was studied from three viewpoints: namely, as being due to (a) early toxic effects on the capillaries, (b) bombardment of sensory impulses from the traumatized region, or (c) local loss of fluid into the damaged region.

a. Since large doses of histamine were necessary to cause death of the animal and also since histamine is removed rapidly from the blood stream of the rat, it would seem that histamine was not the causative factor in this type of shock.

No immediate capillary dilatation was seen to occur in the mesentery or hepatic capillaries when the rubber bands were released. When the loss of fluid was minimized by wrapping the legs tightly, the capillary bed did not differ from that of the normal control animal over a six-hour period of observation following the cutting of the bands. Thus, there was no positive evidence for the liberation of a toxic substance causing immediate capillary damage in this type of shock.

b. Section of the lumbar portion of the spinal cord with needling of the distal segment of the cord did not prolong the lives of the animals in the rubber band type of trauma and, therefore, the bombardment of sensory impulses from the traumatized region would seem to play a minor role in the causation of this type of shock.

c. Wrapping the hind legs tightly with adhesive tape just before the rubber bands were cut, minimizing the local loss of fluid, did prevent the onset of shock as was confirmed by the normal respiratory rate, the normal capillary circulation, the general condition of the animal, and the normal results of hematocrit and red blood cell studies.

Temporary wrapping of the legs for one hour after the bands were cut was not of any benefit.

5. Fluids were given intravenously to the animals at the time the rubber bands were cut. In all these cases, there was much more edema in the legs and pelvis than was seen in the untreated occlusive circulatory type of shock.

a. Ringer's solution enabled the animals to live a little longer than the controls and necessitated one additional dose of pentobarbital sodium.

b. Whole blood permitted the animals to live longer than the controls, necessitating two to four additional doses of pentobarbital sodium. One animal in this group lived for the six-hour period

one-fourth of the total volume of blood removed. The protein content of the concentrated serum and plasma varied from 15 to 20 per cent, that of the normal from 4 to 6 per cent. In several instances, as others have noted,⁷ where concentrated and even normal plasma was administered rapidly, the animals exhibited severe tetany, evidently due to a lowering of the free calcium ion concentration by the considerable amounts of infused sodium citrate. No such effects were observed when normal or concentrated serum was given at comparable rates. The results of the experiments are summarized below.

1. *Blood Pressure.*—The blood pressure rose to near normal levels in all four groups of animals, but with normal serum or plasma the response was more rapid and more pronounced. Those receiving the normal material responded maximally in four to fifteen minutes, after injection, compared to fifteen to thirty minutes in those receiving the concentrated infusion. Another significant observation was the apparent overburdening of the heart by rapidly infused concentrated solutions. This was manifested by a transient drop in the diastolic pressure and slowing of the heart during, and shortly after, such infusions.

The animals treated with concentrated solutions were unable to maintain their blood pressures when subsequent small amounts (10 to 20 c.c.) of blood were withdrawn one hour after the infusion.

2. *Carbon Dioxide Content of the Blood.*—The carbon dioxide content seemed to be a far more accurate criterion for the degree of shock, extent of recovery, and prognosis than the blood pressure. Often a dog whose blood pressure and circulating time had returned to normal after infusion had a carbon dioxide content of 10 to 25 volumes per cent and, subsequently, its condition deteriorated.

Following hemorrhage, the dehydrated dogs usually developed more rapidly a severe degree of shock as indicated by a lower CO_2 . After infusion, in the dehydrated dogs the CO_2 did not return as well as in the normal animals. In general, the effect of normal serum or plasma was superior in both groups to that of the concentrated solutions, as reflected by the higher level to which the CO_2 rose following administration of the former.

3. *Plasma Volumes.*—Plasma volumes, in general, were increased significantly in all four groups of animals following infusion. Despite the increase in plasma volumes, the dogs receiving the concentrated infusions failed to survive as long as those animals receiving normal infusions. This was particularly pronounced in the dehydrated animals. Apparently, the gain in plasma volume and the improvement in circulation following infusions with concentrated solutions were achieved by an extreme and unphysiologic withdrawal of extravascular fluid and, consequently, damage to vital organs and functions may have resulted. It would, thus, seem paradoxical to restore circulating volume and at the same time severely damage the tissues by a therapeutic measure.

THE EFFECTS OF CONCENTRATED SERUM IN CONTRAST TO ISO-OSMOTIC PLASMA UPON NORMAL AND DEHYDRATED DOGS IN SHOCK*

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HUMAN plasma and serum are being prepared and used extensively at the present time. It has been advocated by some¹⁻³ that concentrated plasma protein solutions should be used in the treatment of shock; others⁴ have reported that concentrated and normal protein solutions are of equivalent value in the treatment of experimental post-hemorrhagic shock; still others⁵ have found that concentrated plasma is of no prophylactic or therapeutic value in experimental shock. In view of these conflicting reports and in view of the use of large amounts of concentrated plasma protein solutions in the armed forces, a thorough understanding of the comparative effects of concentrated and normal plasma is needed. Furthermore, in view of the fact that dehydration of combatants is almost inevitable, it is necessary to evaluate the therapeutic effects of normal and concentrated plasma or serum in relation to the state of hydration of the individual. The purpose of this preliminary communication is to present our laboratory experience on the use of normal and concentrated plasma or serum in normal and dehydrated animals. On the basis of this experience, we feel that concentrated blood protein solutions must be used circumspectly, especially in dehydrated individuals.

Shock was produced in dogs by graded hemorrhage, a procedure which has been found to deplete fluid reserves severely.⁶ The state and severity of shock was judged by general condition, circulating time, plasma volume, hematocrit, carbon dioxide content of the plasma, and blood pressure. Essentially two groups of dogs were studied, each group containing at least twelve animals: (a) Normal dogs transfused with normal or with fourfold concentrated canine serum or plasma; (b) dehydrated dogs transfused with normal or with fourfold concentrated canine serum or plasma.

An equivalent amount of protein was restored to all animals, the only difference in the infusions being the water content. Normal serum or plasma was infused to these animals in an amount equal to the total volume of blood removed during the graded hemorrhage at a rate of 50 to 100 c.c. per minute. The fourfold concentrated solutions were given at a rate of 50 c.c. per minute in an amount equal to approximately

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SURGICAL EXCISION OF PRIMARY TUMOR OF LIVER (HARMARTOMA) IN INFANT SEVEN MONTHS OLD WITH RECOVERY

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PRIMARY tumor of the liver in infants is extremely rare but various pathologic types have been described, the most common and most malignant being the primary liver cell carcinoma. Small hemangiomas of the liver are found occasionally at autopsy as incidental findings. They rarely produce symptoms of clinical significance. Of the benign tumors reported, the solitary adenoma is best known; this usually arises from the right lobe of the liver and may reach considerable size. Hamartoma of the liver in infants is another type of benign tumor described in the foreign literature by two authors, each reporting one patient, the diagnosis being made at autopsy in each case. Dr. Ladd of Boston has operated upon two such patients, one of whom survived the operation. Both patients were under one year of age. It has been emphasized by Albrecht, that in the "hamartumors," a very different developmental disturbance proceeds, namely, an excessive development of one tissue of one organ or the retention of the tissue in an embryonal state. Ladd has also stated that this tumor is really not neoplastic but should be regarded rather as development of abnormally placed liver tissues which are attempting to form liver substance but yet not attaining the complete pattern of the normal organ. The mass contains imperfectly formed liver lobules, biliary ducts, and possibly blood vessel networks in a purposeless arrangement. Mitotic figures are rare, there is no tendency to invasion of the surrounding tissues, and metastases do not occur. The mass may be encapsulated and merge with the liver substance. The following case is presented.

CASE REPORT

The patient, a white female, 7 months old, was first seen on Jan. 16, 1942. Five weeks previous to this date, a questionable mass had been noticed midway between the right upper and lower quadrant of the abdomen. Since the first examination, the mass had increased in size but produced no symptoms except occasional vomiting. There had been no loss of weight. From the clinical findings it was thought that this mass might be either a Wilms' tumor of the kidney or a tumor of the liver.

An intravenous pyelogram showed the kidney, pelvis, and calices to be normal but there was a questionable enlargement of the right lobe of the liver. Subse-

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4. *Clinical Conditions and Survival Times.*—The clinical condition and survival time of the normal as well as the dehydrated dogs infused with normal plasma or serum was distinctly superior to the comparable groups receiving the concentrated material.

CONCLUSIONS

1. Concentrated plasma or serum was found to be less effective in the restoration from shock and in maintenance of life thereafter than was normal plasma or serum.

2. The state of hydration was an extremely important factor, in the ability of an animal to withstand shock and its response to therapy. Dehydrated animals developed a more profound state of shock. Their response to plasma or serum infusions, and particularly to concentrated solutions, was decidedly poorer than that of normal animals.

3. Therefore, it can be anticipated that when concentrated plasma or serum is administered, and particularly to dehydrated individuals, the degree and duration of improvement are apt to be incomplete and transient. If only concentrated serum or plasma is available, additional normal plasma or saline solution should be administered simultaneously, or at the earliest possible moment.

4. The amount of citrate contained in plasma may be sufficient to produce tetany if administered rapidly in large amounts.

REFERENCES

1. Cohn, E. J.: Reported at the American Human Serum Association, Cleveland, 1941. Mudd, S., and Thalhimer, Wm.: *Blood Substitutes and Blood Transfusion*, Springfield, Ill., 1942, Charles C Thomas, Publisher.
2. Hill, J. M., Muirhead, E. E., Ashworth, C. T., and Tigertt, W. D.: *J. A. M. A.* 116: 395, 1941.
3. Muirhead, E. E., Ashworth, C. T., and Hill, J. M.: *SURGERY* 12: 14, 1942.
4. Magladery, J. W., Solandt, D. Y., and Best, C. H.: *Brit. M. J.* 2: 249, 1940.
5. Mahoney, E. B., Kingsley, H. D., and Howland, J. W.: *Surg., Gynec. & Obst.* 74: 319, 1942.
6. Levinson, S. O., Neuwelt, F., and Necheles, H.: *J. A. M. A.* 114: 455, 1940.
7. Ashworth, C. T., Muirhead, E. E., and Hill, J. M.: *Am. J. Physiol.* 136: 194, 1942.

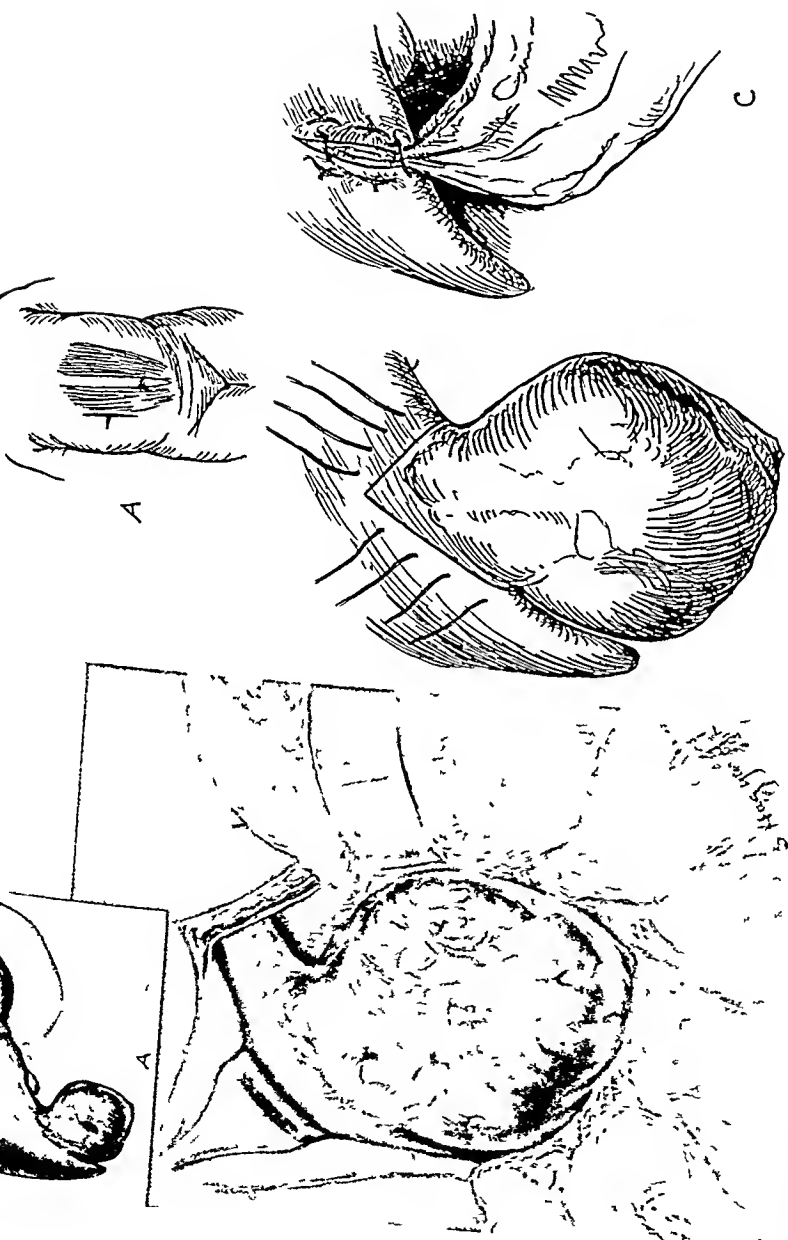


Fig 3.—A, Illustration of size and location of liver tumor. B, Drawing which demonstrates method of isolating tumor preliminary to excision.

Fig 4.—A, Type of incision. B, Illustration of method of inserting sutures and the line of excision of tumor. C, Omentum placed in liver wound and fixation of omentum with chromic sutures.



Fig. 2.—Film taken after evacuation of barium enema. Note the density which appeared continuous with the liver shadow; the liver border is drawn in with solid line.



Fig. 1.—Retrograde pyelogram reveals a normal appearance of the right kidney, pelvis, and calyces but the right ureter is displaced medially.

quently, the patient was cystoscoped and a filament-like catheter was introduced into the right ureter and was injected with an opaque media.

Following the cystoscopy and pyelogram studies, a barium enema showed the ascending colon and cecum to be displaced medialward, underlying the spinal area.

From these findings, a diagnosis of probably primary tumor of the right lobe of the liver was made and surgical intervention advised.

On Jan. 21, 1942, a laparotomy was performed under ether anesthesia. The peritoneal cavity was entered through a high right pararectus incision, with later conversion to a T type of incision. On introducing the hand into the right upper quadrant, a mobile tumor was palpated at the outer margin of the right lobe of the liver and it could be delivered into the operative wound. On gross examination, its surface was quite vascular with large veins on the anterior surface and was classified as a hepatoma. Gauze pads were placed in the right upper quadrant isolating the tumor proper (Fig. 3).

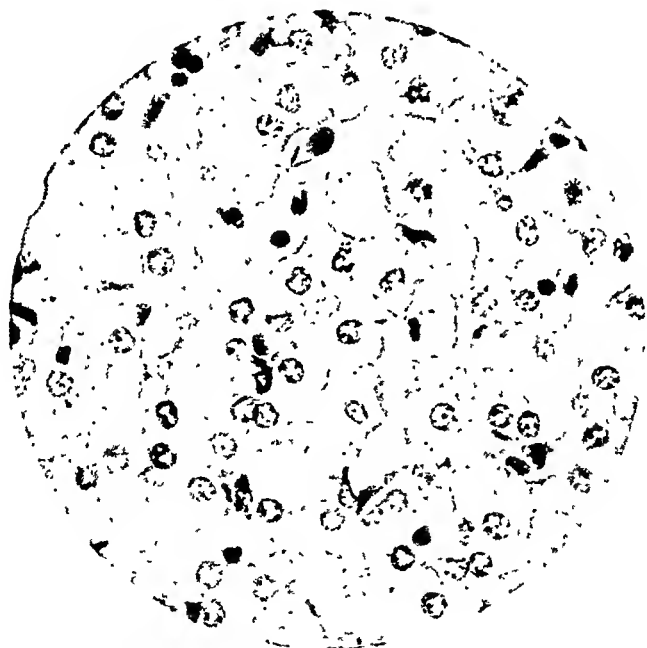


Fig. 7 (H. P.).—Many large hepatic cells with oval or round nuclei are seen; there is vacuolization of the liver cells and no regular arrangement. No mitotic figures are present.

Through-and-through chromic catgut sutures were placed in the liver substance approximately 0.5 cm. away from the borders of the tumor. The tumor was excised with the cautery knife as illustrated in Fig. 4, B. Hemostasis was accomplished by touching the raw surface of the liver with the Bovie coagulating blade. The free edge of the greater omentum was tucked into the operative defect in the liver and anchored in place by the catgut sutures (Fig. 4, C). At this point, the patient showed evidence of moderate surgical shock which was quickly overcome by a transfusion of 100 c.c. of blood. The abdomen was closed in layers using 0 chromic for the peritoneum, and interrupted silk for the fascia and skin. The postoperative course was uneventful and the patient was discharged on the tenth day after operation. On the last examination, May 2, 1942, she was in excellent health.

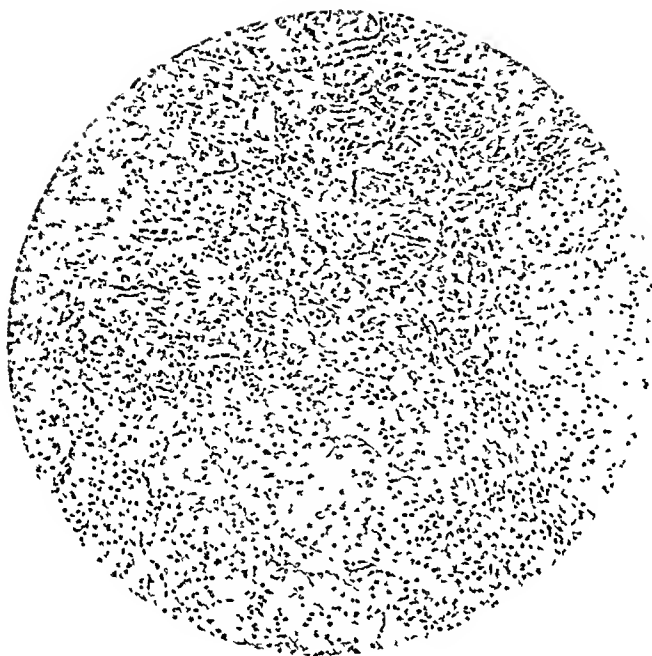


Fig. 6 (L. P.)—There is a Y formation of bile-duct proliferation and in the right half of the field are multiple vacuolated liver cells.

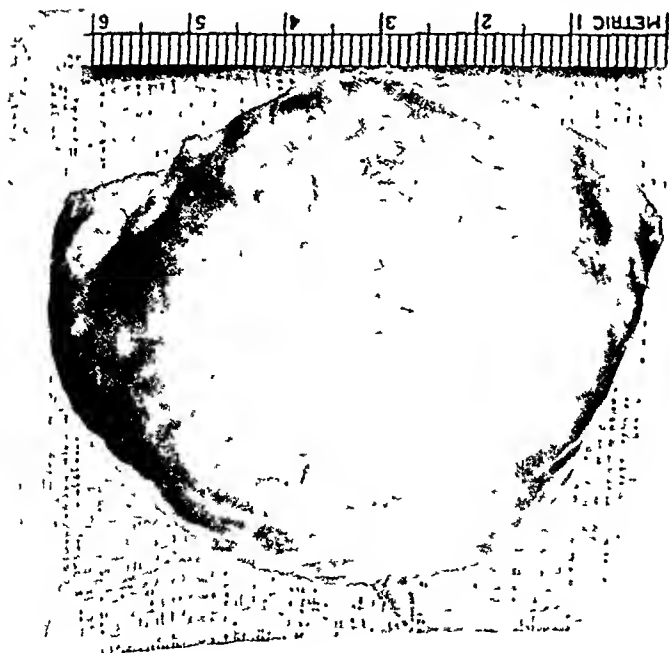


Fig. 7.—The gross specimen removed at operation had the appearance of liver tissue but was encapsulated. The weight of the tumor was 60 Gm., the normal liver of a baby this age weighs approximately 250 Gm.

GASTRIC SECRETORY DEPRESSANT IN GASTRIC JUICE*

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THE discovery of a gastric secretory depressant factor in gastric juice of patients with achlorhydria and gastric carcinoma,¹ and achlorhydria and pernicious anemia² was described in previous reports. The acid gastric juices of patients not presenting these diseases and which were employed in control studies were also found to contain this factor but in obviously much lower concentrations. This led to the hypothesis that the factor was perhaps a normal constituent of gastric juice and was present in increased concentrations in the achlorhydric gastric juices of patients with the above diseases. Further studies were carried out to obtain more data on this question.

METHODS

The same procedures were followed as in the previous work. Subtotal gastric pouches cannulated to the exterior were made in dogs. A month or more later the animals received intravenous injections of neutralized human gastric juices (10 to 20 c.c.) in order to immunize them from febrile reactions due to such injections, since rapid rises in temperature will themselves induce a transitory achlorhydria. Some animals do not become fever resistant as a result of these injections but the acid-secreting mechanism of the gastric pouch does become immune to the inhibitory influence of fever.

With the animals thus prepared, experiments were conducted as follows: The animal, placed upon a table, is fed lean meat and when vigorous secretion from the cannulated pouch obtains, the test solutions or suspensions are injected intravenously and the gastric juice then collected at 10-minute intervals, the volume is noted, and free and combined acidity are titrated, using $\frac{1}{10}$ N - NaOH and Toepfer's reagent and phenothaleine as indicators. Frequent rectal temperatures are obtained to ascertain any unusual rise in temperature that might invalidate the experiment. The animals are also fed meat, forcibly if necessary, at 30- to 40-minute intervals to insure continued physiologic stimulation for secretion of gastric juice. If, as a result of an injection, achlorhydria occurred the experiment was continued until there was a return to preinjection levels of volume and acidity. As in the previous studies, the arbitrary method for recording results was as follows: \pm , reduction in 10-minute secretion volume to 3 drops or less for at least

*This work was conducted under a grant made by the International Cancer Research Foundation, Philadelphia, Pa., for the study of the physiology of the cancerous stomach.

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The microscopic studies as reported by Dr. Plinn F. Morse were as follows. This tumor consisted of irregular lobules of large liver cells arranged in cords with clear vacuolated or acidophilic granular cytoplasm, round to oval nuclei, and a few definite nucleoli. There was moderate fatty degeneration of individual liver cells. The lobules were separated by dense fibrous connective tissue bands in which there was a marked proliferation of the bile ducts with some infiltration into the surrounding hepatic parenchyma. These bile duct radicles were evidenced by cuboidal cells with prominent nuclei, clear cytoplasm, and small tubules with empty lumina. There was no bile stasis. Distinct mitotic figures were not seen in either the hepatic or bile duct cells.

Microscopic Diagnosis.—Liver cell hamartoma or solitary hepatoma (Ewing).

SUMMARY

Complete excision of a primary encapsulated tumor of the liver (hamartoma) in an infant seven months old, with recovery, has been described. The recognition of tumors of the liver in infants is important. All such patients deserve exploratory laparotomy because, in spite of the fact that liver tumors in infants carry a poor prognosis, occasionally a benign tumor such as the one described will be found. Complete surgical removal will offer a good prognosis. Hamartoma tumor of the liver can be considered benign for the following reasons: (1) It is well encapsulated and has embryonal characteristics, (2) it shows no tendency to invade neighboring tissue, (3) on microscopic examination no mitotic figures are found, (4) metastases do not occur, and (5) symptoms arise only from the progressive growth of the tumor with subsequent displacement of neighboring structures.

REFERENCES

1. Schmelling, J. W.: Rare Case of Congenital Multiple Tumors of Liver (Hamartomas) in Infant 4 Months Old, *Nederl. Tydschr. v. Geneesk.* 78: 3566, 1934.
2. Baccarini, Luigi: Contributo allo studio della patogenesi del "fegato policistico" *arch. ital. di chir.* 43: 92-114, 1936.
3. Ladd, W. E., and Gross, R. E.: *Abdominal Surgery of Infancy and Childhood*, Philadelphia, 1941, W. B. Saunders Company.
4. Ladd, W. E.: Personal communication to authors.

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20 minutes with persistence of free acid; ++, achlorhydria for 10 to 20 minutes; +++, achlorhydria for 30 to 50 minutes; +++, achlorhydria for 60 minutes or more.

Precipitation of the Active Factor.—Numerous attempts were made to obtain an active fraction (containing the secretory depressant) of the gastric juice by various types of precipitation. It was observed that an addition of four volumes of absolute alcohol to neutralized juice yielded a white flocculent precipitate which contained the secretory depressant. This method was employed in all of the following studies. the quantity of the precipitate obtained varied for equal volumes of juice. After addition of the alcohol, the mixture was placed overnight in the refrigerator. The next morning as much as possible of the clear supernatant liquid was decanted and the remainder centrifugated. The precipitate was then dried in air and resuspended in 10 to 20 c.c. distilled water for injection.

SERIES I

To Determine Whether the Gastric Secretory Depressant Factor is Present in Dog's Gastric Juice.—Pouch gastric juice was collected from a given animal which was fed meat. The samples were pooled and stored in a large bottle. When the desired volume was obtained it was neutralized to litmus with NaOH (care being taken not to reach alkalinity because this frequently inactivated the factor) and precipitated as described above with alcohol. The precipitate of a small volume was injected as a first experiment, to be followed in a few hours on the next day by injection of the precipitate of a much larger volume. When achlorhydria developed, the latent period varied from twenty to fifty minutes, sometimes longer. In each case the precipitate was obtained from the juice of the dog used in the experiments.

The results are summarized in Table I. They show that the smaller or moderate doses were without effect but that the precipitates of large quantities of juice contained sufficient of the factor to cause transitory inhibition of secretion volume and disappearance of acidity. The prolonged achlorhydria of five hours and twenty minutes observed in one experiment is quite unusual. The negative experiments, five of a total of fourteen where 800 c.c. or more of the juice was used, suggests a marked variation in the concentration of the factor in the pouch juice obtained.

SERIES II

To Observe Whether the Gastric Secretory Depressant Is Present in Large Quantities of Neutralized Acid Human Gastric Juice From Patients Not Presenting Gastric Cancer or Pernicious Anemia.—The juice was obtained from patients subjected to routine histamine tests for gastric secretion in both the outpatient and hospital divisions. Only acid juices were employed and these were filtered through gauze before precipitation. When quantities exceeding 150 c.c. were employed, several samples from different patients were pooled.

In this series of observations "one dose" was arbitrarily chosen as the 80 per cent alcoholic precipitate of neutralized juice, the volume of the juice being equal to 1 c.c. per kilogram weight of the dog employed. The weights of the animals employed varied from 7 to 12 kg. The results of the experiments are summarized in Table II. The progressive increase in incidence of positive experiments paralleling the increase in volume of juice whose precipitate was injected indicates the presence of the gastric secretory depressant in relatively low concentrations in the gastric juice. Fig. 1 is a graph showing secretory depression following intravenous injection of the alcoholic precipitate of 200 c.c. of pooled samples of acid human gastric juice. Further experience showed that the 80 per cent alcoholic precipitate of 500 c.c. of neutralized acid human juice produced transitory achlorhydria in the pouched dogs in over 90 per cent of the experiments, of which more than twenty-five were performed.

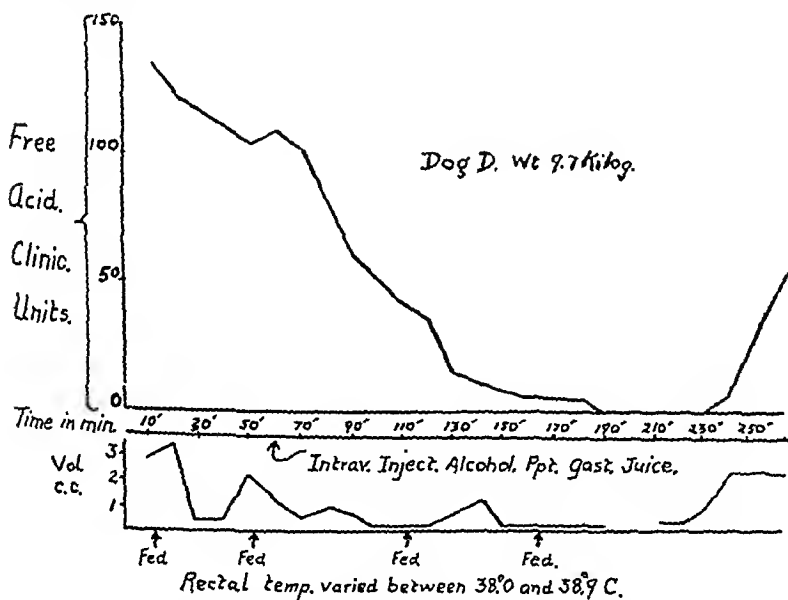


Fig. 1.—Graph showing reduction of acidity and finally transient achlorhydria, with depression of volume of secretion of dog's gastric pouch following intravenous injection of 200 c.c. of water in which was suspended an 80 per cent alcohol precipitate of 200 c.c. of neutralized acid human gastric juice (pooled samples obtained by histamine stimulation). In this period for the development of achlorhydria following injection of the gastric juice was unusually prolonged.

SERIES III

To Observe the Presence of the Gastric Secretory Depressant in Human Achlorhydric Gastric Juice From Patients not Presenting Gastric Carcinoma or Pernicious Anemia.—The achlorhydria juices were obtained in a similar manner as for Series II described above. Because the volumes of such juice obtained from a given patient are not as large as where acid juice is secreted, experiments with large volumes

were not performed. The results obtained are summarized in Table III. The incidence of positive experiments with smaller doses is appreciably greater than that obtained with comparative volumes of samples of

TABLE I

OBSERVATIONS ON THE INDUCTION OF ACHLORHYDRIA IN DOGS BY 80% ALCOHOL PRECIPITATE OF THE DOG'S OWN JUICE

DOG	RESULTS WITH PPT. OF SMALL VOLUME		RESULTS WITH PPT. OF LARGER VOLUMES	
	C.C. OF SAMPLE	ACHLORHYDRIA	C.C. OF SAMPLE	ACHLORHYDRIA
Lady	10	-	115	-
Wal.	12	-	78	-
Pep.	10	-	80	-
Rom.	15	-	500	-
Lady	12	-	600	-
Wal.	12	-	800	+++ (40 minutes)
Wal.	12	-	1000	++ (20 minutes)
Osw.	10	-	900	+++ (40 minutes)
Wal.	12	-	900	+++ (40 minutes)
Ging.	12	-	1000	++ (10 minutes)
Wal.	12	-	1000	-
Rom.	15	-	1000	++++ (5 hours, 20 minutes)
Rom.	15	-	1000	-
Wal.	12	-	1000	-
Wal.	12	-	1000	-
Longf.	12	-	1000	+
Rom.	12	-	1000	+
Ging.	12	-	1000	-
Longf.	12	+	1000	++++ (90 minutes)

TABLE II

ACHLORHYDRIA PRODUCED IN DOGS BY INJECTION OF 80% ALCOHOL PRECIPITATE OF NEUTRALIZED HUMAN ACID GASTRIC JUICE*

QUANTITY OF JUICE PRECIPITATED	NO. OF EXPERIMENTS NEGATIVE	NO. OF EXPERIMENTS SHOWING ACHLORHYDRIA OR MARKED SUPPRESSION OF SECRETION VOLUME	PER CENT OF EXPERIMENTS "POSITIVE"
Single "dose"	64	16	20
Triple "dose"	29	14	33
Four to five "doses"	12	9	42
Six to eight "doses"	24	17	55
Nine to sixteen "doses"	12	20	66

*From patients not presenting gastric carcinoma or pernicious anemia.

One "dose" = precipitate of volume of juice equal to 1 c.c. per kilogram weight of the animal employed.

TABLE III

ACHLORHYDRIA PRODUCED IN DOGS BY INJECTION OF 80% ALCOHOL PRECIPITATE OF ACHLORHYDRIC HUMAN GASTRIC JUICES*

QUANTITY OF JUICE PRECIPITATED	NO. OF EXPERIMENTS NEGATIVE	NO. OF EXPERIMENTS SHOWING ACHLORHYDRIA OR MARKED SUPPRESSION OF SECRETION VOLUME	PER CENT OF EXPERIMENTS "POSITIVE"
Single "dose"	20	10	30
Triple "doses"	19	20	52

*From patients not presenting gastric cancer or pernicious anemia.

Each experiment represents one sample of juice from one individual patient.

acid juice suggesting a greater concentration of the depressant factor associated with achlorhydria.

Some studies were conducted upon the properties of the secretory depressant; it was observed to be destroyed by boiling for five minutes; it was found not to dialyze across a cellophane membrane; alkalization of the juice inactivates the secretory depressant.

DISCUSSION

Extensive control experiments have been performed and reported^{1, 2} to show that the gastric secretory depression observed in the experiments is not artifactual incident to intravenous injection of gastric juice. The nature and significance of the gastric secretory depressant demonstrated in gastric juice of both dogs and humans remains obscure, but it is suggested that it may represent a normal physiologic mechanism for gastric secretory inhibition. Support for this hypothesis is afforded by the fact that it appears to be present in greater quantity in achlorhydric juice. An alternate explanation is that it is secreted at more or less constant rate by some cells of the gastric mucosa and that in achlorhydria it appears to be more concentrated in the juice because the total volume of the latter is reduced as compared with stomachs secreting acid gastric juice.

SUMMARY

By a standard physiologic method for the study of factors affecting gastric secretion, a gastric secretory depressant has been demonstrated to be present in dog's gastric pouch juice, acid human gastric juice, and achlorhydric gastric juice from patients not presenting gastric cancer or pernicious anemia.

Taking into account previously recorded studies, this factor appears to be present in lower concentrations in the above types of juice than in the achlorhydric gastric juice of patients with carcinoma of the stomach or with pernicious anemia.

REFERENCES

1. Brunshwig, A., Clarke, T. H., Prohaska, J. van, and Schmitz, R. L.: A Secretory Depressant in the Achlorhydric Gastric Juice of Patients With Carcinoma of the Stomach, *Surg., Gynec. & Obst.* 70: 25-30, 1940.
2. Brunshwig, A., Prohaska, J. van, Clarke, T. H., and Kandel, E.: A Secretory Depressant in the Gastric Juice of Patients With Pernicious Anemia, *J. Clin. Investigation* 18: 415-422, 1939.

THE HALSTED RADICAL MASTECTOMY

FIVE-YEAR RESULTS IN 246 CONSECUTIVE OPERATIONS AT THE SAME CLINIC

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THE effectiveness of a method of treating cancer of the breast can best be judged by following its results in a consecutive series of patients over a period of five years and more. This report deals with such a series and includes 240 patients, all cared for in the same institution. It is an extension of a report made by R. D. McClure, in 1931.¹⁷ In each case the primary growth was removed by radical mastectomy, following the method of Halsted. In eleven cases a subsequent carcinoma was found in the opposite breast. Six of these patients were subjected to a second radical mastectomy, while five had a simple mastectomy. All 240 patients were operated upon between 1918 and 1935 inclusive, so that the follow-up of the living patients covered at least five years. In only six cases, however, (2.5 per cent) are our follow-up records incomplete.* Most of these patients had evidence of metastases when last seen, and for statistical purposes have been considered as dead from carcinoma.

The criteria of operability were much the same as in other clinics. Radical operations were not advised in patients with known distant metastases, advanced local breast cancer, or ulcerating lesions, or in patients in poor general condition. Thirteen cases involving demonstrable supraclavicular metastases were operated upon, although this complication usually was considered a criterion of inoperability. Deep fixation of the carcinoma to the pectoral fascia was not considered a contraindication in the absence of ulceration.

The average age of the group of 240 patients was 51.2 years, 28 and 77 years being the extremes. In 75 cases the ages of the patients fell in the fifth decade, while the sixth and seventh followed closely, with 69 and 47 cases, respectively. Age did not appear to affect the percentage of cases with axillary node involvement nor did it appear to affect the percentage of five-year survivals to any significant degree (Table I). This is similar to Shore's²¹ findings at St. Luke's Hospital in New York.

Only one case in this series was a male (0.45 per cent), a lower incidence than that commonly reported in similar series. Horsely¹² reported 4 cases of carcinoma of the breast in the male to 359 in the female, or 1.1 per cent. Stout²⁴ found the proportion of 6 to 349, or 1.7 per cent, while Judd and Morse¹³ found 17 cases of carcinoma of the male breast to 1,751 cases of carcinoma of the female breast, or 0.9 per

*For the high percentage of patients followed, thanks are due the Detroit Board of Health and its field worker, Mrs. Helen Andries, and also Miss Ruby Cook, who handled all correspondence and recording.

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cent. Judd and Morse concluded that carcinoma of the male breast was a highly malignant type of neoplasm and that radical operation was not as satisfactory as in females. The patient in our case lived seven years and ten months following operation and manifested several sites of metastases, among them the tonsil and the cervical and axillary nodes.

TABLE I
CASES GROUPED ACCORDING TO AGE

AGE	20-29	30-39	40-49	50-59	60-69	70-79	TOTAL
Number of cases	1	36	75	69	47	12	240
Percentage	0.4	15.0	31.2	28.7	19.5	5.0	100
Number of cases with axillary metastases	1	26	48	40	28	6	149
Percentage	100	72.0	64.0	58.0	57.0	50.0	62.1
Number of five-year survivals	0	10	40	34	19	8	111
Percentage	0	28.5	53.0	49.0	40.5	66.6	46.0

A history of trauma was elicited in 15 of the 251 tumors removed, giving a percentage of 5.9. Twenty-seven patients (11.2 per cent) stated that one of their immediate relatives had had cancer, while in 13 cases (5.4 per cent) the cancer was said to have been in the breast.

The known duration of the presenting symptoms was analyzed to determine if a higher percentage of axillary metastases was found in those patients who did not present themselves until some time elapsed after they were conscious of their disease. In those cases where the symptoms were present for a month or less, axillary metastases were present in 55.3 per cent. If the symptoms were present from one to six months, 59.8 per cent of the patients had axillary metastases, while those who let their symptoms develop over six months had axillary metastases in 62.7 per cent of the cases. The percentage of five-year survivors in each group diminished as the length of time the symptoms were present increased, regardless of whether or not axillary metastases were present (Table II). This gives added evidence to support the dictum that carcinoma should be treated early and adequately for the best results.

Lewis and Rienhoff,¹⁵ and Kunath¹⁴ did not find any definite correlation between the duration of symptoms and the length of life after

TABLE II
A COMPARISON OF FIVE-YEAR SURVIVALS ACCORDING TO DURATION OF SYMPTOMS

DURATION OF SYMPTOMS	AXIL- LARY METAS- TASES	NO AXIL- LARY METAS- TASES	% AXIL- LARY METAS- TASES	NO. 5-YEAR SURVIVALS		% 5-YEAR SURVIVALS	
				AXIL- LARY METAS- TASES	NO AXIL- LARY METAS- TASES	AXIL- LARY METAS- TASES	NO AXIL- LARY METAS- TASES
1 month or less	26	21	55.3	9	15	34.6	71.4
1 to 6 months	64	43	59.8	20	29	31.2	67.4
Over 6 months	54	32	62.7	14	21	25.8	65.6
No data	6						

operation. Greenough and Taylor⁸ found that in their different groups of cases based on metastases, the preoperative duration of symptoms was longer in the patients that did not survive the five-year period. Their statistics, like those of Lewis and Rienhoff,¹⁵ contain several cases with a preoperative history of a tumor for two or more years with a high incidence of five-year survivals. This is not surprising when one considers that these are low-grade malignancies, else they would not have lived long enough to be operated upon.

In comparing the two breasts as to the frequency of the primary tumor, the left breast was found involved oftener than the right, by 13.8 per cent. The right breast was involved in 106 cases, while the left in 140 cases, or 43.1 and 56.9 per cent, respectively. However, in regard to the quadrants of the breast another situation existed. The upper outer quadrant was by far the most frequent site involved. One hundred and nineteen of the tumors in this series were located in that quadrant. The second most common site for the location of tumors was under the areola. Analysis of the location of the primary tumor with reference to five-year survivals showed that the upper outer quadrant and the line directly above the areola had the lowest percentage, while the lower outer quadrant had the highest (Table III).

TABLE III
LOCATION OF TUMOR IN BREAST

LOCATION	NUMBER OF CASES	FIVE-YEAR SURVIVALS	PERCENTAGE
Upper outer quadrant	119	45	37.8
Upper inner quadrant	34	18	52.6
Lower outer quadrant	20	13	65.0
Lower inner quadrant	14	9	64.2
Under areola	40	19	47.5
Directly above nipple	8	3	37.5
Medial to nipple	2	1	50.0
No data	9	3	33.0

No correlation was found between the postoperative duration of life and the size of the tumor removed. When the various sized tumors were subdivided into groups with and without axillary metastases, a great difference in the percentages of five-year survivals was noted, which contributes more evidence to the fact that the presence or absence of axillary metastases is still our best prognostic sign. In the 246 radical mastectomies, the pathologist was able to locate metastases in the axillary nodes in 152 cases (61.7 per cent). Harrington¹¹ found that 61.6 per cent of the 5,830 cases he reported had axillary involvement.

Clinical examination revealed palpable axillary nodes in 145 of our cases. Of these, 111 (76.5 per cent) contained demonstrable metastases. In 97 cases where no nodes were palpable, on clinical examination, metastases were later demonstrated in 38 (39.1 per cent). This makes the error of clinical impression of axillary involvement 23.5 per cent when nodes are palpable and 39.1 per cent when no nodes are palpable.

Greenough and Taylor⁸ and Shore²¹ note the marked error in the pre-operative diagnosis of the presence of axillary metastases and their percentage of error is almost the same as ours, namely, 32 and 34.2 per cent respectively. The above figures of error in the clinical examination of the axilla for metastases support a strong feeling we have that the value of information gained from axillary palpation is slight at best and decidedly not worth the danger to the patient from searching or repeated efforts to find lymph nodes.

The radical removal of the breast for mammary carcinoma used in this series is essentially the one developed by Halsted⁹ and Meyer.¹⁸ The Halsted skin incision was also used for the most part. Skin grafts were not performed in all cases, however, as described by Halsted. A plastic closure was used in 176 cases and the Thiersch graft in 46 cases. In 24 cases a Thiersch graft was not used, but instead a secondary pinch graft was used after a few days' convalescence from the radical mastectomy.

Local skin recurrence occurred in 15 per cent of the cases. The patients with plastic closures in this series had a local skin recurrence rate of 5.5 per cent and 16 per cent, depending upon whether or not axillary metastases were present. When a skin graft was done, the recurrence rates in the skin were 8.3 and 27 per cent (Table IV). One possible

TABLE IV
A COMPARISON OF TYPES OF CLOSURE AND LOCAL SKIN RECURRENCES

	NO. OF CASES	NO. OF RECURRENCES	PERCENTAGE
Plastic Closure:			
No axillary metastases	23	4	5.5
Axillary metastases	82	13	16.0
Skin Grafts:			
No axillary metastases	24	2	8.3
Axillary metastases	67	18	27.0
Regardless of Closure:			
No axillary metastases	97	6	6.1
Axillary metastases	149	31	20.8
Total	246	37	15.0

reason for the difference between the recurrence rates with the different closures is that the larger primary tumors, or tumors attached to skin or fascia, required larger areas of skin in the incision and by the same token were probably the most malignant neoplasms. Lewis and Rienhoff¹⁵ reported the percentage of local recurrences in 447 radical mastectomies. They found 30.1 per cent local recurrences when the Thiersch graft was used and 39.1 per cent after the plastic closure was done. Our statistics made to determine the correlation between the amount of skin excised at operation and percentage of five-year survivals showed no correlation which could be explained on this basis. The group without axillary metastases, which had a large area of skin removed, showed the

greatest number of five-year survivals (83 per cent). However, when axillary metastases were present, the percentage of five-year survivals dropped to 21 per cent, which was even lower than the group in which the plastic closure had been done (Table V).

TABLE V
A. COMPARISON OF TYPES OF CLOSURE ACCORDING TO FIVE-YEAR SURVIVALS

	NO. OF CASES	NO. OF FIVE- YEAR SURVIVALS	PERCENTAGE
Plastic Closure:			
No axillary metastases	73	49	67.0
Axillary metastases	82	28	34.0
Skin Graft:			
No axillary metastases	24	20	83.0
Axillary metastases	67	14	21.0
Regardless of Closure:			
No axillary metastases	97	69	71.0
Axillary metastases	149	42	28.0
Total	246	111	45.0

Patients with postoperative distant metastases form an interesting group for the metastases may appear at any time after the operation and frequently only after the lapse of several years without symptoms. In the case of bone metastases, pain is probably the earliest symptom and was occasionally present from four to six months before demonstrable x-ray changes could be detected. We were able to diagnose bone metastases by x-ray in 50 cases (20.8 per cent). The spine was the most frequent site of bone metastases, with the ribs next in frequency (Table VI). Metastatic lesions were found in the lungs and pleura

TABLE VI
BONES INVOLVED IN METASTASES

Spine	33	Mandible	3
Ribs	20	Scapula	3
Pelvis	16	Fibula	2
Femur	16	Tibia	1
Humerus	4	Clavicle	1
Sacrum	3	Maxilla	1
Sternum			1

somewhat more frequently than in the bones. These were diagnosed principally by x-ray. However, a few cases were confirmed either by post-mortem examination or microscopic examination of the pleural fluid. Fifty-eight cases (24.1 per cent) were diagnosed as having pulmonary metastases.

Edema of the arm may occur pre- or postoperatively. When present preoperatively, it is a physical sign of advanced disease. Postoperatively it may occur at any time. It was present in 69 of the cases in this series (28.9 per cent). An interesting feature concerning this was the fact that it was transitory in many cases, and in these cases it frequently

appeared about two or three months after the operation and disappeared after a few months. In a few cases the edema was permanent, but in no case was it incapacitating or disabling. In a few cases it was preceded by a postoperative axillary infection, a recurrence of carcinoma in the axilla, or a thrombophlebitis in the vessels of the arm. Stewart²² stated that he "regarded immediate postoperative edema of the arm as a favorable sign; it indicates that the operation has been thorough, that all the lymphatic structures in the axilla have been removed, and the lymphatic drains of the arm completely interrupted. It usually disappears in from two to four months, but may last longer, and indeed be permanent."

The postoperative mortality in this series was somewhat lower than some reports and higher than those reported in some textbooks. There were seven postoperative deaths in 246 radical mastectomies (2.8 per cent). Three deaths were from pulmonary emboli and two others were patients with marked hypertension who died of myocardial failure. One death was in a 34-year-old woman who had a large breast tumor and fluid in her chest. This did not contain tumor cells and the x-ray examination of the chest did not show a definite metastasis. No post-mortem examination was done, but this patient probably had a small pulmonary metastasis which was present at the time of operation. She lived ten days postoperatively, but the course was steadily downhill. One death was in a patient who had a marked anemia preoperatively. She was given several pre- and postoperative transfusions, but these did not bring her blood count up to normal. Post-mortem examination showed subacute parenchymatous nephritis. The urine preoperatively was negative and her history was not suggestive of nephritis.

Willy Meyer¹⁸ reported four deaths in a series of 125 radical mastectomies (3.2 per cent). Lewis and Rienhoff¹⁵ reported twenty-five deaths following 393 radical mastectomies (6.4 per cent). Stiles²³ states he has had "one death in upwards of 150 patients operated upon." The cause of that patient's death was sepsis. He also quoted Rodman, who collected the results of 2,133 radical mastectomies and found an operative mortality of less than 1 per cent. Handley¹⁰ commented on the low immediate mortality of the operative procedure in the following manner, "Among some hundreds of hospital cases, including cases in paying hospital wards, four deaths have to be recorded." Bloodgood⁴ stated that the operative mortality of radical mastectomy was less than $\frac{1}{2}$ per cent if a supraclavicular dissection was not done as part of the same procedure.

An interesting finding in the follow-up of this series of 240 patients with mammary carcinoma is the high incidence of a second carcinoma. Twelve patients lived long enough following the radical mastectomy to develop a second primary malignancy in another organ or tissue (Table VII). Carcinoma of the skin, cervix, and stomach were the most common. Most of the pathologic specimens of the second malignancy were

TABLE VII
SECOND PRIMARY MALIGNANCY

DATE OF RADICAL MASTECTOMY	SECOND CANCER	DATE OF DEATH
12/29/23	Squamous carcinoma of scalp 10/20/27	7/18/29
1/28/25	Adenocarcinoma of gall bladder 8/23/33	3/ 6/36
2/28/25	Carcinoma of stomach 1/14/30	1/14/30
7/22/26	Carcinoma of cervix 4/7/37	4/29/38
1/23/26	Basal cell carcinoma of skin; post- mortem finding 9/9/36	9/ 9/36
5/26/27	Basal cell carcinoma of skin 5/31/27	3/ 2/32
1/30/28	Carcinoma of colon; post-mortem find- ing 1/14/31	1/14/31
1/24/30	Osteogenic sarcoma; post-mortem find- ing 11/29/39	11/29/39
5/23/30	Carcinoma of ovary January, 1933	January, 1933
2/12/31	Carcinoma of cervix 3/12/35	December, 1935
6/20/32	Carcinoma of bladder January, 1938	3/30/38
2/6/35	Carcinoma of stomach 10/29/36	6/13/37

examined in this hospital; those that were not were reported to us by other institutions in the course of our follow-up. As stated earlier, 11 of the 240 developed a second carcinoma in the opposite breast which could be removed either by simple or radical mastectomy, depending upon the general condition of the patient. Others developed deposits of carcinoma in the other breast along with numerous other metastases, late in the course of the disease. One may always speculate as to whether the second tumor is a new primary or a metastasis. Inasmuch as the microscopic picture of the second tumor in most of the eleven cases was quite similar to that of the first, one would be inclined to favor the theory that the tumors were metastatic.

Although the relationship between chronic cystic disease of the breast and carcinoma cannot be definitely determined by a statistical study, it is interesting to note the frequency with which it was recorded by the pathologist in the description of the breast carcinomas of this series. Twenty-eight of the 251 specimens submitted (11.1 per cent) contained chronic cystic mastitis, and in eight of the cases it appeared that the malignancy might have originated in the area so involved. An independent review of 149 cases of chronic cystic mastitis in which either a local removal of the tumor or simple mastectomy was done showed no case which later developed carcinoma. The follow-up of twenty-five of these cases extended over five years and many from two to four years. Cheate and Cutler⁶ state that breast carcinoma develops from cystiphorous desquamative epithelial hyperplasia (chronic cystic mastitis) in about 20 per cent of the cases of carcinoma. "In the remaining 80

per cent of all carcinoma of the breast it is not so easy to demonstrate the existence of a preliminary benign epithelial neoplasm and further that all signs of a preliminary cystic state are absent." Bloodgood^{2, 3} presents the opposite point of view, believing that carcinoma does not develop more frequently in women with chronic cystic mastitis than in any other group of women in the same age group. He reports three cases of cancer which developed in 128 cases following the removal of an area of chronic cystic mastitis. Stout²⁴ believes there is a definite relationship between chronic cystic mastitis and carcinoma of the breast, but does not go into more detail than to make this statement. MacCallum¹⁶ states "carcinoma growth seems especially common as a sequel of the senile hyperplasia with cyst formation, which is often referred to as chronic cystic mastitis."

There has been much discussion over the merits of roentgen or radium therapy in the treatment of carcinoma of the breast. When one discusses radiation therapy, however, the question comes up as to whether or not it should be given pre- or postoperatively, what dosage should be given, the location of the radiation ports, and whether it should be radium or x-ray therapy. In this series, all radiation therapy was given after a radical mastectomy. It consisted of a course of three treatments which were usually given on consecutive days. Three ports were used, namely, a supraclavicular port, one which included the operated breast area, and the third was directed to the corresponding axilla. Approximately 700 R. units were delivered to the skin with each treatment. The usual filters were $\frac{1}{2}$ mm. of copper and 1 mm. of aluminum.

An attempt was made to compare groups of cases according to the amount of x-ray therapy given. The number of five-year survivals was computed for each group, depending upon the presence or absence of axillary metastases. The greatest percentage of five-year survivals was in the group with no axillary metastases and no irradiation therapy (74.4 per cent). The groups with one, or more than one, series of irradiation therapy and no axillary metastases had almost the same percentage of five-year survivals. In the three groups with axillary metastases there was a suggestive increase in the percentage of five-year survivals when x-ray therapy was used. If no irradiation was used, there was only 21.8 per cent five-year survival, while the percentage rose to 35.8 per cent and 26.8 per cent when x-ray therapy was used (Table VIII).

The cases were analyzed further to determine the effect of x-ray therapy on local skin recurrence. The series was divided into two groups, depending upon whether or not axillary metastases were present, and these were subdivided into the recurrences that had had prophylactic irradiation therapy and those that had not. Skin recurrences were much more frequent in the group that had axillary metastases (20.8 per cent) than in the group that did not (6.1 per cent). Fifty-four of

TABLE VIII

A COMPARISON OF THE EFFECT OF X-RAY THERAPY ACCORDING TO FIVE-YEAR SURVIVALS

NO. OF X-RAY COURSES	NO. OF CASES	NO. OF FIVE-YEAR SURVIVALS	PERCENTAGE
NO AXILLARY METASTASES			
0	43	32	74.4
1	38	26	68.4
2	16	11	68.7
AXILLARY METASTASES PRESENT			
0	55	12	21.8
1	53	19	35.8
2	41	11	26.8

the 97 patients without axillary nodes had x-ray therapy and of these, three (5.1 per cent) developed local skin recurrences. Among the 43 that did not have x-ray therapy, three patients (6.9 per cent) developed local skin recurrences. Ninety-four of the 149 patients with axillary metastases had x-ray therapy, and of this group 23 patients (24.4 per cent) developed local skin recurrences. Among the 55 cases which did not have x-ray therapy, eight patients developed local skin recurrences (14.5 per cent). The type of closure was not taken into consideration in studying the effect of x-ray therapy as the series was so small that it would be questionable if the percentages would give a true picture (Table IX).

TABLE IX

A COMPARISON OF THE PERCENTAGE OF LOCAL SKIN RECURRENCES WITH AND WITHOUT X-RAY THERAPY IN CASES WITH AND WITHOUT AXILLARY METASTASES

	X-RAY THERAPY	NO X-RAY THERAPY	TOTALS
NO AXILLARY METASTASES			
Number of cases	54	43	97
Recurrences	3	3	6
Percentage	5.1	6.9	6.1
AXILLARY METASTASES			
Number of cases	94	55	149
Recurrences	23	8	31
Percentage	24.4	14.5	20.8

In attempting to judge the value of x-ray therapy in this series of cases one must say that no improvement in the number of five-year survivals was noted in the cases without axillary metastases, although a decrease was found in the number of local skin recurrences. However, irradiation therapy did appear to increase the number of five-year survivals in the cases concerned with axillary metastases, but did not appear to affect the percentage of local skin recurrences.

From a review of the cases involving late metastases, either local or distant, one finds convincing evidence that it is in these cases that x-ray therapy finds its greatest usefulness. The results here are difficult to express in percentages, for many times the effects are subjective and symptomatic, but nonetheless important. Pfahler and Parry¹³ reviewed

TABLE X (FROM HARRINGTON)
A COMPARISON OF SURVIVAL RATES ACCORDING TO POSTOPERATIVE IRRADIATION IN THE FOUR GRADES OF MALIGNANCY; UNILATERAL CARCINOMA
IN WOMEN WITH AXILLARY METASTASIS

GROUP	3 YEARS			5 YEARS			10 YEARS			15 YEARS			20 YEARS		
	PATIENTS TRACED*	PER CENT SURVIVALS		PATIENTS TRACED*	PER CENT SURVIVALS		PATIENTS TRACED*	PER CENT SURVIVALS		PATIENTS TRACED*	PER CENT SURVIVALS		PATIENTS TRACED*	PER CENT SURVIVALS	
<i>Concerning 181 patients treated with irradiation and 100 treated without irradiation†</i>															
<i>With irradiation:</i>															
Grade 1	8	100.0		7	100.0		7	71.4		4	25.0		1	0	
Grade 2	143	63.6		136	47.1		112	27.7		93	22.6		16	18.8	
Grade 3	615	52.4		567	34.2		432	16.2		268	9.3		72	5.6	
Grade 4	1293	36.3		1121	23.6		733	12.7		409	6.6		118	4.2	
<i>Without irradiation:</i>															
Grade 1	3	100.0		3	100.0		3	66.7		3	66.7		3	33.3	
Grade 2	46	76.1		46	58.7		43	34.9		39	30.8		33	24.2	
Grade 3	209	43.5		207	26.1		180	12.8		154	7.8		135	3.7	
Grade 4	389	28.5		376	18.4		330	10.9		280	8.2		243	5.8	
<i>Concerning 409 patients treated with irradiation and 284 without irradiation†</i>															
<i>With irradiation:</i>															
Grade 1	66	98.5		54	100.0		29	89.7		10	70.0		6	66.7	
Grade 2	162	92.0		126	87.3		58	56.9		9	33.3		2	0	
Grade 3	244	85.2		180	73.3		76	44.7		21	28.6		6	0	
Grade 4	133	76.7		97	62.9		47	44.7		13	15.1		4	25.0	
<i>Without irradiation:</i>															
Grade 1	83	94.0		62	88.7		32	78.1		25	64.0		20	60.0	
Grade 2	121	86.3		109	76.1		63	58.7		38	36.8		34	26.5	
Grade 3	120	74.2		115	56.5		80	42.5		58	37.9		57	31.6	
Grade 4	104	60.6		101	53.5		89	39.3		69	29.0		67	22.4	

*Only patients operated upon and traced for the different periods are included in this table.

†Grade of malignancy was not stated.

ninety-three cases of patients with carcinoma of the breast to determine the value of x-ray therapy. They used postoperative x-ray therapy in forty-one cases. Comparing the percentages of five-year survivals in the cases where there were no axillary metastases, they found a difference of 2 per cent, namely, 89 per cent five-year survivals, when postoperative x-ray therapy was used and 87 per cent when it was not used. This difference is certainly not significant, yet they state, "It is our opinion that operation combined with irradiation will practically double the results as compared with operation alone."

Schreiner²⁰ reviewed 283 cases of carcinoma of the breast. In 46 patients without axillary metastases and treated with irradiation therapy after a radical mastectomy, 65 per cent were classified as five-year survivals. When axillary metastases were present the five-year survivals fell to 23 per cent.

Evans and Leucutia⁷ report 50 per cent five-year survivals in the group including patients with and without axillary metastases who had had a radical mastectomy, followed by x-ray therapy. They concluded that "irradiation therapy plays a paramount role in the treatment of mammary carcinoma both as an adjunct to surgery in the operable and as a primary method in the inoperable cases."

Harrington¹¹ divided 4,504 cases into those with patients with and without axillary metastases and then subdivided the groups into those with and without x-ray therapy and according to the four grades of the tumor, pathologically. This study led to very interesting results inasmuch as the follow-up was conducted over a period of twenty years. Harrington concluded "that irradiation therapy has not been any great adjunct to radical surgical treatment but may be of benefit in cases of higher grades of malignancy." (Table X.)

Shore²¹ reported the follow-up of 375 cases in a series of 418 patients who had had a radical mastectomy. One-hundred and ninety-six were given routine postoperative prophylactic x-ray treatment; of these, 36 developed local recurrences (18.3 per cent). He does not state the percentage of these that had axillary metastases. The greatest number of recurrences in another table, however, was found in the patients with axillary metastases, regardless of x-ray therapy. His conclusions were that "postoperative irradiation rarely cures and usually does not prevent local recurrences and therefore does not decrease the mortality from cancer of the breast. It does, however, undoubtedly prolong some lives so that a few patients who would otherwise have died within five years after operations have survived several more months to be classified in the five-year group."

Adair¹ reports an interesting study of 2,467 operable cases.

"The conclusions from these statistics were that irradiation, either before or after the operations in cases with axillary involvement, had a decided value in this clinical group."

TABLE XI (FROM ADAIR)

471 had operation alone		
857 had preoperative irradiation followed by radical surgery		
485 had the radical mastectomy followed by irradiation		
413 had irradiation alone		
214 began treatment and then went elsewhere		
27 had a local removal of cancer followed by irradiation therapy		
2467 total		
	<i>Five-Year Results</i>	
	NO AXILLARY INVOLVEMENT (%)	WITH AXILLARY INVOLVEMENT (%)
Operation alone	68	25
Preoperative irradiation followed by radical surgery	65	29
Radical surgery followed by postoperative irradiation	70	31
Irradiation alone	25	9

Brooks and Daniels⁵ have reported an unusually high percentage of five-year survivals in a series of 72 radical mastectomies. They do not draw any conclusions, however, concerning irradiation therapy.

TABLE XII (BROOKS AND DANIELS)

	GROUP	CASE	LIVING AND WELL	PERCENTAGE
Given roentgenotherapy	I*	3	2	66.6
	II†	7	3	42.8
	III‡	9	1	11.1
Not given roentgenotherapy	I*	10	10	100.0
	II†	21	6	28.5
	III‡	22	3	13.6

*Carcinoma confined to breast.

†Carcinoma confined to breast and inferior axillary lymph nodes by microscopic study.

‡Carcinoma in breast and in axilla or near chest wall at operations.

SUMMARY AND CONCLUSIONS

1. A statistical study was made of 240 consecutive, unselected patients with mammary carcinoma who had radical mastectomies at the Henry Ford Hospital and of whom 234 have been accurately followed.
2. Chronic cystic mastitis was not present in a sufficient number of cases to imply any significant correlation between this pathologic process and cancer.
3. Carcinoma of the male breast occurred less frequently than in reports from other clinics.
4. The presence or absence of metastases at operation dominated all other clinical factors influencing prognosis.
5. Age did not appear to be an important factor per se.
6. A history of trauma occurred infrequently and a familial tendency to cancer did not occur frequently enough to seem significant.

7. The duration of symptoms before operation appeared to influence adversely the postoperative survival period.

8. Survival seemed to vary slightly with the quadrant of the breast affected.

9. The size of the tumor was not as important an indication of prognosis as was the presence or absence of axillary metastases.

10. Such a considerable error was found in the ability to detect and evaluate axillary nodes clinically that we believe palpation of the axilla should be discouraged as a diagnostic aid on account of the danger of massaging tumor cells out of involved glands.

11. Late lymphedema of the arm, tending to disappear after a time, was the most frequent form in which this complication occurred.

12. The postoperative mortality of 2.8 per cent in this series is discussed.

13. The five-year survivals of this series are discussed with particular reference to the presence or absence of axillary metastases and the use or nonuse of x-ray therapy.

14. X-ray therapy did not improve five-year survivals in those patients without axillary metastases. It seemed to add slightly to the survival of patients with axillary metastases.

15. The great value of x-ray therapy in the treatment of metastases, particularly those of bone, is stressed.

REFERENCES

1. Adair, F. E.: A Consideration of Recent Additions to Clinical and Experimental Knowledge of Breast Conditions, *West. J. Surg.* 48: 645-661, 1940.
2. Bloodgood, J. C.: The Pathology of Chronic Cystic Mastitis of the Female Breast, *Arch. Surg.* 3: 445-542, 1921.
3. Bloodgood, J. C.: The Blue-domed Cyst in Chronic Cystic Mastitis, *J. A. M. A.* 93: 1056-1059, 1929.
4. Bloodgood, J. C.: The Breast, A Treatise on Regional Surgery, Vol. I, Philadelphia, 1917, The Blakiston Company, p. 630.
5. Brooks, B., and Daniels, R. A., Jr.: The Present Status of the "Radical Operation" for Carcinoma of the Breast, *Ann. Surg.* 3: 688-699, 1940.
6. Cheate, G. L., and Cutler, Max: Tumors of the Breast, Philadelphia, 1931, J. B. Lippincott Company, p. 92.
7. Evans, W. A., and Leucutia, T.: Deep Roentgen Ray Therapy of Mammary Carcinoma, *Am. J. Roentgenol.* 42: 866-881, 1939.
8. Greenough, R. B., and Taylor, T. W.: Cancer of the Breast: End-Results, *New England J. Med.* 210: 831-835, 1934.
9. Halsted, W. S.: Developments in the Skin Grafting Operation for Cancer of the Breast, *J. A. M. A.* 60: 416-418, 1913.
10. Handley, W. S.: Cancer of the Breast, Ed. 2, New York, 1922, Paul B. Hoeber, Inc., p. 218.
11. Harrington, S. W.: Results of Radical Mastectomy in 5026 Cases of Carcinoma of the Breast, *Pennsylvania M. J.* 43: 413-427, 1940.
12. Horsely, J. S., Jr.: Benign and Malignant Lesions of the Male Breast, *Ann. Surg.* 109: 912-920, 1939.
13. Judd, E. S., and Morse, H. D.: Carcinoma of the Male Breast, *Surg., Gynec. & Obst.* 62: 15-18, 1926.
14. Kunath, C. H.: Problem of Carcinoma of the Breast, *Arch. Surg.* 41: 66-78, 1940.

15. Lewis, D., and Rienhoff, W. F., Jr.: A Study of the Results of Operations for Cure of Cancer of the Breast, *Ann. Surg.* 95: 336-400, 1932.
16. MacCallum, W. G.: *Textbook of Pathology*, Ed. 6, Philadelphia, 1936, W. B. Saunders Company, p. 1160.
17. McClure, R. D.: A Study of Cancer of the Breast, *South. S. A.* 44: 372, 1931.
18. Meyer, W.: Cancer of the Breast, *Surg., Gynec. & Obst.* 24: 553-577, 1917.
19. Pfahler, A. E., and Parry, L. D.: Results of Roentgen Therapy in Carcinoma of the Breast, *J. A. M. A.* 94: 101-105, 1930.
20. Schreiner, A. F.: Results of Treatment of Causes of the Breast Cancer, Philadelphia, 1931, J. B. Lippincott Company, p. 269.
21. Shore, R. R.: Carcinoma of the Breast, *Surg., Gynec., & Obst.* 71: 515-519, 1940.
22. Stewart, F. T.: Amputations of the Breast by a Transverse Incision, *Ann. Surg.* 62: 250-251, 1915.
23. Stiles, H. J.: Operations for Carcinoma, *Oxford Surgery* 4: part 1, 89, 1918.
24. Stout, A. P.: *Human Cancer*, Philadelphia, 1932, Lea & Febiger, p. 254.

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REFERENCES

1. Adair, F. E.: *A Consideration of Recent Additions to Clinical and Experimental Knowledge of Breast Conditions*, West. J. Surg. 48: 645-661, 1940.
2. Bloodgood, J. C.: *The Pathology of Chronic Cystic Mastitis of the Female Breast*, Arch. Surg. 3: 445-542, 1921.
3. Bloodgood, J. C.: *The Blue-domed Cyst in Chronic Cystic Mastitis*, J. A. M. A. 93: 1056-1059, 1929.
4. Bloodgood, J. C.: *The Breast, A Treatise on Regional Surgery*, Vol. I, Philadelphia, 1917, The Blakiston Company, p. 630.
5. Brooks, B., and Daniels, R. A., Jr.: *The Present Status of the "Radical Operation" for Carcinoma of the Breast*, Ann. Surg. 3: 688-699, 1940.
6. Cheate, G. L., and Cutler, Max: *Tumors of the Breast*, Philadelphia, 1931, J. B. Lippincott Company, p. 92.
7. Evans, W. A., and Leventis, T.: *Deep Roentgen Ray Therapy of Mammary Carcinoma*, Am. J. Roentgenol. 42: 866-881, 1939.
8. Greenough, R. B., and Taylor, T. W.: *Cancer of the Breast: End-Results*, New England J. Med. 210: 831-835, 1934.
9. Halsted, W. S.: *Developments in the Skin Grafting Operation for Cancer of the Breast*, J. A. M. A. 60: 416-418, 1913.
10. Handley, W. S.: *Cancer of the Breast*, Ed. 2, New York, 1922, Paul B. Hoeber, Inc., p. 218.
11. Harrington, S. W.: *Results of Radical Mastectomy in 5026 Cases of Carcinoma of the Breast*, Pennsylvania M. J. 43: 413-427, 1940.
12. Horsely, J. S., Jr.: *Benign and Malignant Lesions of the Male Breast*, Ann. Surg. 109: 912-920, 1939.
13. Judd, E. S., and Morse, H. D.: *Carcinoma of the Male Breast*, Surg., Gynec. & Obst. 62: 15-18, 1926.
14. Kunath, C. H.: *Problem of Carcinoma of the Breast*, Arch. Surg. 41: 66-78, 1940.

clarified. Hageman, studying the pathologic lesions of mice intoxicated with sulfanilamide, noted a mild fibroblastic foreign-body reaction about crystals of the drug, when it was administered intraperitoneally as a suspension in saline. Key and Frankel injected supersaturated solutions of sulfanilamide, sulfapyridine, and sulfamethylthiazole into body cavities and observed that the peritoneal surface presented little departure from normal. Jackson and Collier, using dogs, found that sulfanilamide administered intraperitoneally did not induce any cellular response in the peritoneal fluid. Small amounts of free fluid were noted, but no hyperemia or exudate was observed and the peritoneal surfaces appeared entirely normal. From these reports, it would seem that sulfanilamide, whether in solution or in crystalline form, produces little if any peritoneal reaction.

EXPERIMENTAL METHOD

The experimental animal chosen was the 100 Gm. albino rat. This choice was made because (1) the peritoneal responses of the white rat to various substances have been investigated intensively; (2) the peritoneal fluid of this animal normally has a high cellular content, and (3) the albino rat withstands laparotomy very well.

Peritoneal fluid was obtained in all instances by puncture with a clean, fine, glass capillary pipette. The fluid which entered the pipette by positive pressure was deposited on a clean glass slide and a sufficient amount was drawn into a hematologic white cell pipette for the total cell count. The remainder of the fluid was spread evenly over the slide for subsequent staining in order to determine the differential distribution of the cells. These air-dried films were stained with a May-Grünwald-Giemsa combination: thirty seconds in May-Grünwald stain, thirty seconds in equal parts May-Grünwald stain and Hayden's buffer at pH 6.4, and three to four minutes in buffer-diluted Giemsa stain, 1.5 drops to the milliliter of buffer.

The total and differential cell counts were recorded for the peritoneal fluid of each experimental animal prior to any experimental procedure. Following this, laparotomy was performed through a midline incision with the animal under ether anesthesia. One hundred milligrams of a powdered sulfonamide compound was distributed evenly about the peritoneal cavity and immediate suture was done with fine silk. In one group of rats, simple laparotomy was performed without the intraperitoneal implantation of any of the sulfonamide compounds. These animals constituted the control series. Total and differential cell counts were made on the peritoneal fluid of all animals on which operation was performed. The cell counts were made at twenty-four-hour intervals for periods ranging from five to seven days. Animals were killed at intervals by light etherization and exsanguination for pathologic study.

Estimations of the total quantity of peritoneal fluid were made by absorbing all free fluid into previously weighed pieces of filter paper. Increases of the weights of the filter paper were determined and accepted as weight of fluid.

The following drugs were implanted intraperitoneally in doses of 1 Gm. per kilogram of body weight: sulfanilamide, sulfathiazole, sulfapyridine, sulfadiazine, sulfamethyldiazine and sulfanilylguanidine.

RESULTS

Throughout the entire period of the experiment, no deaths occurred and no toxic manifestations were noted.

THE PERITONEAL RESPONSE TO LOCALLY IMPLANTED CRYSTALLINE SULFONAMIDE COMPOUNDS*

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THERE is little need to recount the victories of the sulfonamide compounds in the field of surgery. The proper systemic use of these drugs has made deep inroads into the number of deaths attributable to infectious surgical complications: deaths that have plagued the most dexterous and conscientious surgeons. The local implantation of the sulfonamide compounds, in an attempt to exert their effects more fully, is an instance of medical empiricism now fully backed by clinical and laboratory confirmation. It is accepted generally that in high local concentration the bacteriostatic value of these drugs is enhanced. The metabolism of bacteria is altered, their growth is inhibited, their ability to form toxins and necrobiotic substances is impaired, and all this to the end that a mobilized cellular defense mechanism is able to overwhelm the attenuated organisms. It is conceded that the defense mechanisms of the body are necessary to the complete therapeutic activity of these drugs; however, the direct effect of local sulfonamide therapy on tissue defense has received little attention, although knowledge of possible relation between the two is essential to the rational employment of these drugs as local chemotherapeutic agents.

Most significant of these newer local applications has been the use of crystalline sulfonamide compounds within the peritoneal cavity. In this fashion the surgeon has been provided with a possible means of direct frontal attack on the problem of peritonitis. Clinical and experimental evidence of therapeutic efficacy has been accumulating; yet little actually is known of the peritoneal response to these substances. Therefore, it has been the purpose of this study to determine the peritoneal response to crystalline sulfonamide compounds, with special regard to their possible effects on the local peritoneal defense mechanism.

LITERATURE

Since the report of Dees, the topic of intraperitoneal sulfonamide therapy has received ever-increasing notice in the literature. Clinical reports have been followed closely by laboratory confirmation. The weight of favorable opinion has swept aside prejudice and inertia, and the value of intra-abdominal chemotherapy appears to be established in the minds of most physicians. However, the relation of this new weapon to the defensive forces of the peritoneal cavity has not been

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report for differential data calculated without inclusion of neutrophils. This method of calculation gives, it would seem, a truer picture of cellular relation in the peritoneal fluid than does the differential count in

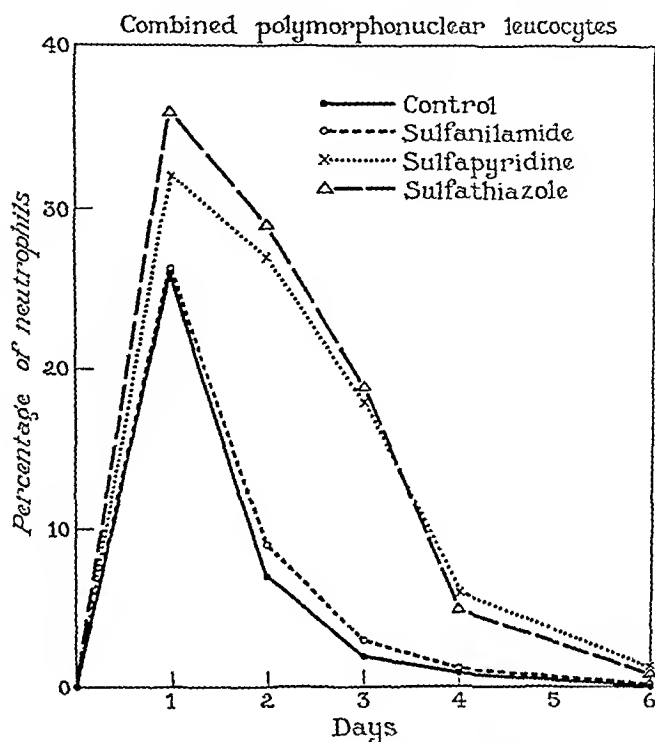


Fig. 1.—Percentage distribution of the neutrophils of the peritoneal fluid following laparotomy and the implantation of certain sulfonamide compounds.

TABLE II
PERITONEAL RESPONSE TO LAPAROTOMY
MEAN VALUES OF SIXTEEN ANIMALS

HOURS AFTER OPERATION	TOTAL CELL COUNT PER CUBIC MILLIMETER OF PERI- TONEAL FLUID	DIFFERENTIAL CELL COUNTS							
		ACTUAL				RELATIVE			
		NEUTRO- PHILES	MONO- CYTES	EOSINO- PHILES	MAST CELLS	MONO- CYTES	EOSINO- PHILES	MAST CELLS	LYMPHO- CYTE PHAGO- CYTE RATIO
Control	39,300	0	71	23	6	71	23	6	23:77
24	83,800	26	53	19	2	72	25	3	22:78
48	59,000	7	69	23	1	72	26	2	22:78
72	57,600	2	67	28	3	69	28	3	22:78
120	55,200	1	70	26	3	71	26	3	23:77
168	61,300	0	70	28	2	70	28	2	

which neutrophils are included. Thus, it is apparent that the relative numbers of mononuclear cells and eosinophiles are unchanged by laparotomy and the ratio of mononuclear phagocytic elements to lymphocytes remains unaltered (Fig. 2).

As may be seen (Table I) the mononuclear cells are the predominant cellular elements in the peritoneal fluid of the white rat. These have been divided empirically in this study, the nonphagocytic lymphocytes being placed in one group and the potentially phagocytic and usually larger mononuclear cells in the other. This latter group, referred to hereafter as mononuclear phagocytes, contains the typical monocytes and the true clasmatocytes as well as the various transitional forms. Differentiation of these mononuclear phagocytes was not attempted. It is notable that neutrophils were not found in the normal peritoneal fluids; these cells, when present, are certain indications of a past or present pathologic condition. The eosinophilic leucocytes are subject to rather wide and inexplicable variations, while the mast cells almost disappear in the face of peritoneal irritation, a fact intensively investigated by Webb.

TABLE I

THE PERITONEAL FLUID OF THE NORMAL 100 GM. WHITE RAT MEAN VALUES OF FORTY-EIGHT ANIMALS

Total cells per cubic millimeter:	39,300
1. Mononuclear leucocytes:	71 per cent of total cell count
a. Large mononuclears (phagocytes):	70 per cent of all mononuclear cells
b. Lymphocytes:	30 per cent of all mononuclear cells
2. Eosinophiles:	23 per cent of total cell count
3. Mast cells (basophiles):	6 per cent of total cell count
4. Neutrophiles:	0
Weight of peritoneal fluid:	285 mg. (six determinations)

Throughout the period of the experiment, certain abnormalities were encountered in the cytologic characteristics of the peritoneal fluid of approximately 30 per cent of the animals used. Such animals, though usually healthy in other respects, were not included in the compilation of these data. The apparent reasons for these variations from the normal were (1) dehydration; (2) peritoneal infection, usually the result of visceral puncture, and (3) endemic enteritis.

Control Group: Peritoneal Response to Simple Laparotomy.—This group comprises sixteen animals and a brief of the important data is shown in Table II. As noted previously by Higgins and Montgomery, simple laparotomy, when carefully performed, causes little actual change in the cytologic picture of the peritoneal fluid. Most striking is the influx of neutrophils (Fig. 1), a fact which is mirrored in the transient increase of the total cells per cubic millimeter of fluid. The mononuclear cells at first glance seem to undergo a decrease but further analysis shows that this diminution of mononuclears (as well as eosinophiles) is only relative to the influx of neutrophils. The inclusion of the neutrophile in any differential study merely adds an extrinsic variable which distorts the true ratio of the cells normally found in the peritoneal fluid, a fact appreciated by Webb in his statistical analysis. The term, "relative differential count," has been used in this

of sulfanilamide, the only observations of importance were a lack of adhesions, except as in the control series, and some enlargement of the spleen. This organ, which was almost black, confirmed previous observations of Machella and Higgins, and showed neither microscopic changes nor increased iron deposits.

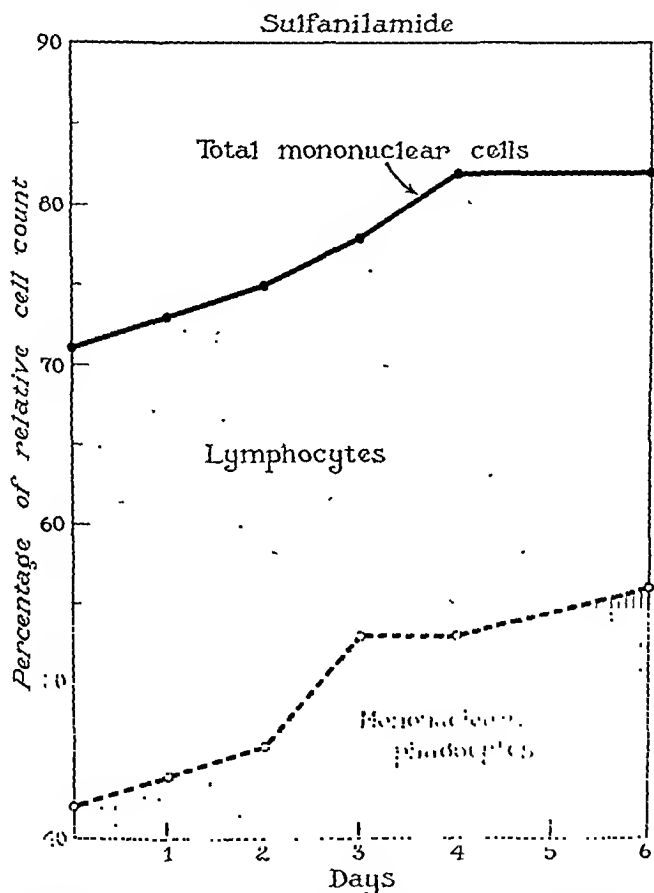


Fig. 3.—Percentage of mononuclear components of the total number of cells, exclusive of neutrophils, following the intraperitoneal implantation of sulfanilamide.

The Response Within the Peritoneal Cavity to Sulfathiazole.—Eighteen animals were used in this series. Sulfathiazole remained grossly visible for three to five days. During the first forty-eight hours, the drug generally appeared as agglutinated masses, floating freely and not evidencing any tendency to serosal attachment or peritoneal damage. Any undissolved clumps of the drug were taken up subsequently by the omentum and had dissolved completely therein by the third to fifth day. In this connection, several features are of note. First, the more uniform the implantation of the drug about the peritoneum, the less likely are undissolved clumps of the drug to remain for subsequent omental disposal. Second, the use of crystals instead of the powdered

The Response Within the Peritoneal Cavity to Sulfanilamide.—Twelve animals were used in this series. Although the amounts of sulfanilamide were rather large, gross evidence of the drug was not visible six to eight hours after its introduction into the peritoneal space. There was no hyperemia of either visceral or parietal peritoneum and a transitory initial increase of the quantity of fluid had disappeared in twenty-four

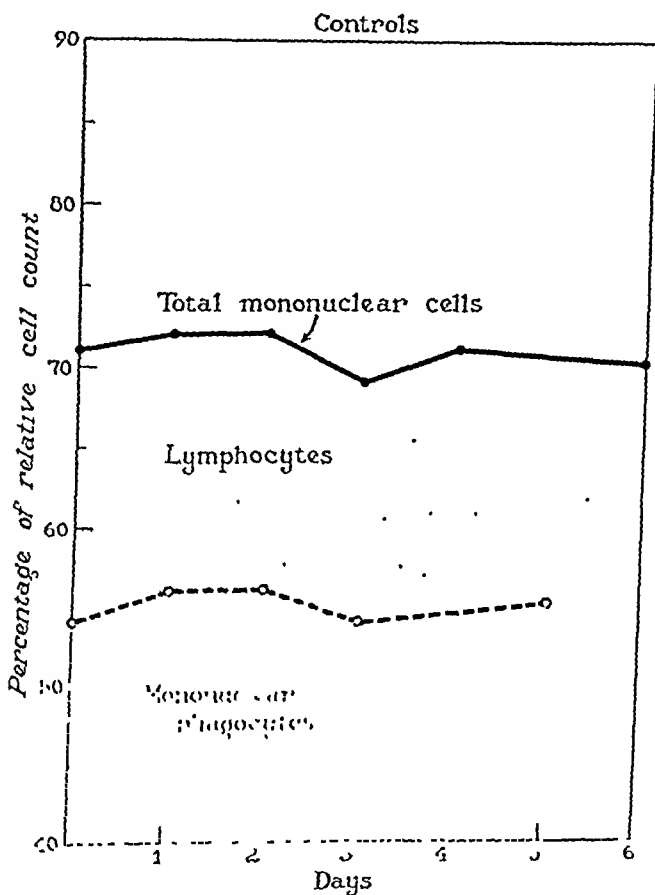


Fig 2—Percentage of mononuclear components of the total number of cells, exclusive of neutrophils, following laparotomy

hours. The cellular reaction to sulfanilamide had two important characteristics: (1) The neutrophile response was not beyond levels observed in control animals (Fig. 1). Thus, it appears that sulfanilamide when introduced intraperitoneally does not induce any acute inflammatory response. (2) There did occur, however, a low-grade stimulation of the large mononuclear phagocytic cells, together with a gradual increase of 10 per cent in their number over a six-day period (Fig. 3). This reaction is typical of extremely mild peritoneal irritation. At post-mortem examination, seven to fourteen days after the introduction

At necropsy, ten to fourteen days after the introduction of sulfathiazole, the peritoneal cavities were essentially normal. There were no notable adhesions, although a very occasional focus of milky fibroblastic proliferation occurred in regions where a mass of the drug had dissolved slowly in contact with the liver. The spleens were moderately black and enlarged in about 75 per cent of the animals, recalling the condition previously described in all the animals receiving sulfanilamide.

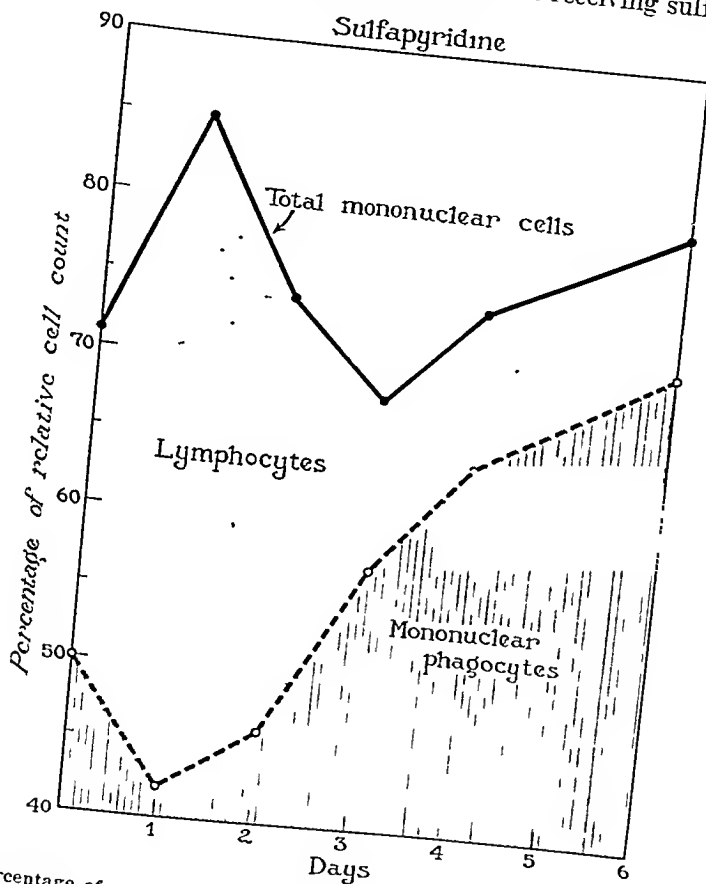


Fig. 5—Percentage of mononuclear components of the total number of cells, exclusive of neutrophils, following the intraperitoneal implantation of sulfapyridine.

The Response Within the Peritoneal Cavity to Sulfapyridine.—Twenty animals were used in this series. In these experiments sulfapyridine proved to be a strong peritoneal irritant. As late as twenty-four hours after its introduction into the peritoneal cavity, the actual quantity of peritoneal fluid recovered was 470 mg. as compared with 215 mg. for controls on which operation had been performed. Furthermore, the agglutinated masses of drug were sufficiently irritating to produce serosal attachment. These clumps of drug were walled off rapidly

drug greatly facilitated the implantation, because the powder tends to mass itself in damp clumps, like confectioners' sugar, while the crystalline form distributes itself more evenly like granulated sugar. In either instance, the peritoneal cellular response was identical. This reaction was characterized by (1) minimal serosal damage, as evidenced by lack of adhesions; (2) a moderate and prolonged neutrophilic response, as compared with control levels (Fig. 1); (3) an immediate and marked increase of the number of mononuclear phagocytes (Fig. 4), in which

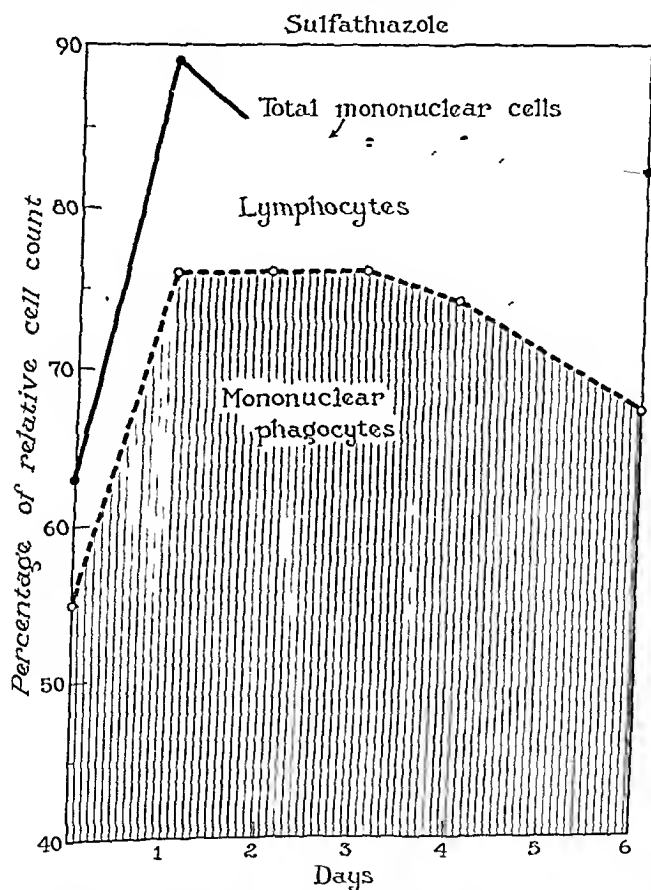


Fig 4.—Percentage of mononuclear components of the total number of cells, exclusive of neutrophils, following the intraperitoneal implantation of sulfathiazole

there was evidence of extreme activity (large size, multinucleation, cytoplasmic inclusions and vacuolization, and rare mitotic figures), and (4) a noticeable increase of the total cell count per cubic millimeter of fluid beyond control levels. This not only reflects an actual cellular increment but also shows that the degree of peritoneal irritation had not been severe enough to produce a fluid dilution factor. This latter observation was borne out by actual measurement.

less irritating than sulfapyridine. At twenty-four hours after implantation, masses of sulfadiazine were firmly adherent to adjacent tissue surfaces, lying between the incision and the omentum. However, by the sixth postoperative day, only an occasional remnant of the drug remained undissolved.

The peritoneal reaction to sulfadiazine was characterized by (1) some serosal attachment and damage; (2) a walling off of the agglutinated masses of the drug, to a lesser degree than that produced by sulfapyridine; (3) a noticeable neutrophilic leucocytic reaction; (4) a small initial shower of lymphocytes, together with a rapid and steady increase of the large mononuclear phagocytic cells (Fig. 6), and (5) an inflammatory increase of the quantity of peritoneal fluid to 330 mg. in twenty-four hours, sufficient to produce a notable dilution of the total cells per cubic millimeter. The spleens were normal in all animals.

The Response Within the Peritoneal Cavity to Sulfamethyldiazine and Sulfanilylguanidine.—These drugs were used in small series, six animals for sulfamethyldiazine and twelve for sulfanilylguanidine. The gross peritoneal responses to them were almost identical and somewhat similar to that elicited by sulfathiazole. The drugs evidenced little tendency to serosal damage or attachment, grossly disappeared from the peritoneum in three to five days, and produced cellular responses somewhat like those elicited by sulfadiazine. The spleens were not affected by sulfamethyldiazine, but in approximately 30 per cent of animals receiving sulfanilylguanidine the previously described splenic changes were observed at necropsy.

COMMENT

The sulfonamide compounds are bacteriostatic drugs; their action in the body is to prevent invasion. The summation of their effect is simply an attenuation of virulent microorganisms, holding them in check until the local tissue defenses, long ago perfected by nature, can overwhelm them. Thus, in the final analysis, it is the mustering defensive forces of the body which repel the invader and repair the damage, a fact appreciated by Paracelsus, in 1536. With this in mind, it must be apparent that intraperitoneal sulfonamide therapy is a valuable adjunct to abdominal surgery, but its use does not lessen the responsibilities of the surgeon. Among these responsibilities is the choice of the proper sulfonamide compound for intraperitoneal implantation. Should one postulate an ideal sulfonamide compound for intraperitoneal use, it is certain that the following qualities would be included: (1) The compound should be active against a variety of microorganisms; (2) it should be innocuous to the peritoneum; (3) it should exert a prolonged bacteriostatic effect; (4) it should stimulate the natural local defense mechanism, to complement the attenuating effect of the drug ; bacteria.

among the viscera and by the omentum, and frequently could be seen, fourteen days after implantation, surrounded by foreign-body giant cells. Organizing adhesions were frequent and one instance of partial intestinal obstruction was noted. The cellular reaction was characterized by (1) a response of the neutrophils similar to that induced by sulfathiazole (Fig. 1); (2) an initial shower of lymphocytes, the small round cells of inflammation, followed by a rapid accumulation of mononuclear phagocytic cells (Fig. 5), phenomena which are indicative of

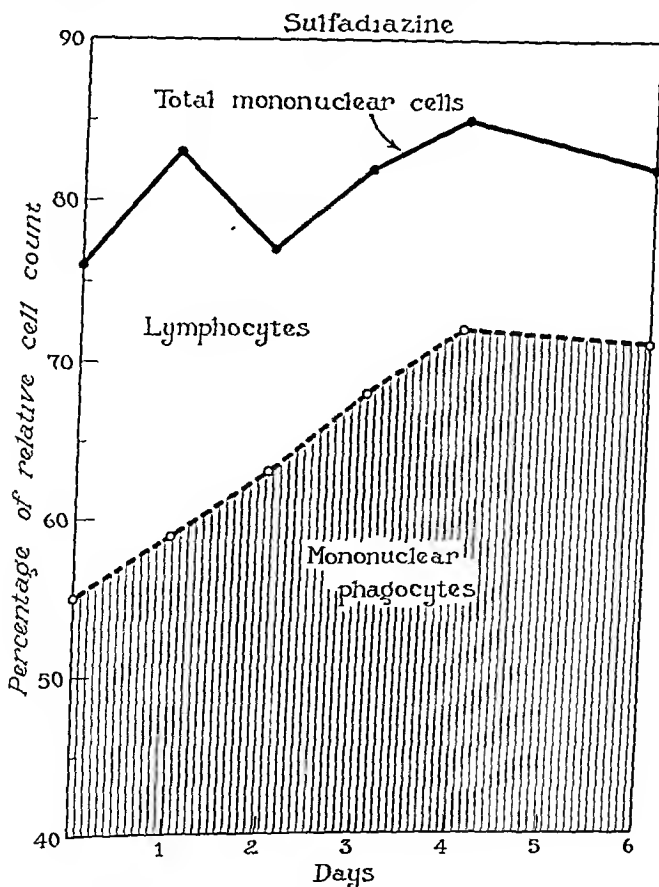


Fig. 6.—Percentage of mononuclear components of the total number of cells, exclusive of neutrophils, following the intraperitoneal implantation of sulfadiazine.

violent peritoneal irritation, as seen in aleuronat peritonitis or following intraperitoneal injection of sodium ricinoleate, and (3) an inflammatory increase of the peritoneal fluid sufficient to cause a noticeable dilution factor in the total cell count per cubic millimeter. At necropsy, the spleens were not notably enlarged but were dark in about 50 per cent of the animals.

The Response Within the Peritoneal Cavity to Sulfadiazine.—This drug was used in a series of six animals and found to be only slightly

Hinshaw and Moses suggest that pigmentation with a sulfhemoglobin compound may be the answer.

SUMMARY

An experimental technique is reviewed for the study of the peritoneal responses to crystalline sulfonamide compounds. Data are presented on the peritoneal responses of the white rat to simple laparotomy and the intraperitoneal implantation of sulfanilamide, sulfathiazole, sulfapyridine, sulfadiazine, sulfamethyldiazine, and sulfanilylguanidine. Each of these drugs produces some peritoneal reaction, as mirrored in the cellular changes which take place in the peritoneal fluid. These reactions, ranging from the meager response to sulfanilamide to the violent responses induced by sulfapyridine, are nonspecific and depend on a foreign-body reaction of the tissues toward the drug itself, as well as on the innate irritant properties of certain of these compounds. The relation of this local tissue response to the efficacy of sulfonamide therapy is stressed. These drugs owe their therapeutic value to properties of bacteriostasis; the actual killing and disposal of the attenuated bacteria are performed by the local cellular defense mechanism. The augmentation of the peritoneal cellular defenses by these drugs in local application is of great value, complementing as it does their bacteriostatic properties. However, the vigorous response initiated by certain of the sulfonamide compounds, especially sulfapyridine, walls them off from the general peritoneal cavity so rapidly as to reduce their effectiveness as bacteriostatic agents. Of the sulfonamide compounds used in this study, it would seem that sulfathiazole has certain advantages as an intraperitoneal chemotherapeutic agent: (1) it is active against a variety of microorganisms; (2) it is innocuous to the peritoneum; (3) it exerts a prolonged bacteriostatic effect, and (4) it stimulates the local cytologic defense mechanism to an effort the equal of any inspired by usual methods of peritoneal vaccination.

REFERENCES

1. Bloom, William: Lymphocytes and Monocytes; Theories of Hematopoiesis, Fibroblasts and Histiocytes. In Downey, Hal: Handbook of Hematology, New York, 1938, Paul B. Hoeber, Inc., p. 373.
2. Dees, J. G.: A Valuable Adjunct in Perforated Appendices, *Mississippi Doctor* 18: 215-217, 1940.
3. Epps, C. H., Ley, E. B., and Howard, R. M.: Treatment of Peritonitis: Intraperitoneal Use of the Sulfonamides Based Upon Animal Experiments, *Surg., Gynec. & Obst.* 74: 176-179, 1942.
4. Feldman, W. H., Hinshaw, H. C., and Moses, H. E.: Personal communication to the author.
5. Gay, F. P., and Clark, A. R.: On Mode of Action of Sulfanilamide in Experimental Streptococcus Empyema, *J. Exper. Med.* 66: 535-548, 1937.
6. Gay, F. P., and Morrison, L. F.: Clasmatocytes and Resistance to Streptococcus Infection: Studies in Streptococcus Infection and Immunity, *J. Infect. Dis.* 33: 338-367, 1923.
7. Hageman, P. O.: Toxicity of Sulfanilamide. A Study of the Pathological Lesions in White Mice, *Proc. Soc. Exper. Biol. & Med.* 37: 119-122, 1937.
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With these four premises in mind, it is apparent from these experimental data that sulfathiazole, of the sulfonamide compounds now in general use, is the most logical choice. It is bacteriostatic against most of the commonly encountered pyogenic microorganisms, and especially against *Streptococcus faecalis* and *Escherichia coli*, those symbiotic invaders so common in peritonitis. It is innocuous to the peritoneum and contiguous structures. It exerts a prolonged action, remaining grossly visible and unattached in the peritoneum for three or four days. Some clinical proof of this lies in a statement by Herrell that levels of this drug of more than 500 mg. per 100 c.c. are maintained readily in the human peritoneal exudate for four to five days following its implantation in quantities of 10 Gm. And lastly, sulfathiazole musters the local defensive forces to an effort that equals any produced by the usual means of intraperitoneal vaccination.

This latter reaction deserves some attention. The cellular responses elicited by the sulfonamide compounds when implanted intraperitoneally are qualitatively those of nonspecific peritoneal irritation. The quantitative differences observed evidently are allied to such factors as solubility and chemical irritation rather than to any possible specific cellular stimulation. The peritoneal response produced by the rapidly dissolving and inert sulfanilamide is meager at best. At the other extreme, the response initiated by the irritating sulfapyridine is so violent that the masses of drug are walled off from the general peritoneal cavity long before their solution is complete. Midway between these two is the peritoneal response to sulfathiazole. This drug seems to act as a slowly dissolving, nonirritating foreign body. Not only does the cellular reaction provide neutrophils as a first line of defense, but, more important, there is a rapid augmentation of mononuclear phagocytes, the real bulwark of cellular defense and the potential building units of reparative processes. Regardless of such factors as omental migration, fluid dilution, and antibody reaction, the mononuclear phagocyte is probably the most important single element in the peritoneal defense. This response to sulfathiazole is the equal of that inspired by methods of peritoneal vaccination, as studied in the rat by Seely, Higgins, and Mann.

The sulfonamide compounds, in local application, offer a means of attack on peritoneal infection, not only therapeutically but also prophylactically. The ability of sulfathiazole to enhance the local cytologic defense mechanism, in conjunction with prolonged bacteriostasis, would seem to make it the sulfonamide compound of choice for intraperitoneal use. This theoretical superiority is being borne out and confirmed by recent studies, especially the controlled experiments on peritonitis of animals by Epps, Ley, and Howard.

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2. Dees, J. G.: A Valuable Adjunct in Perforated Appendices, Mississippi Doctor 18: 215 217, 1940.
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COMPARATIVE BLOOD CONCENTRATIONS OF SULFAGUANIDINE, SULFANILAMIDE, AND SULFATHIAZOLE AFTER ADMINISTRATION ORALLY, PERITONEALLY, AND PLEURALLY TO DOGS

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INTRODUCTION

THE relative rates of absorption of sulfanilamide and sulfathiazole from the gastrointestinal tract, peritoneal cavity, and pleural cavity of dogs have been previously reported from the laboratory of the Medical College of Virginia with a brief discussion of the clinical significance of such observations.^{1, 2} Since the introduction of sulfaguanidine,³ studies have been made as to its bacteriostatic effect on intrapleural application⁴; its local effects on the peritoneal cavity⁵; and its diffusing tendency when placed in wounds.⁶ The fact that sulfaguanidine was regarded as being especially poorly absorbed from the gastrointestinal tract, had a low systemic toxicity, and had been found to be effective against several types of pathogenic organisms,³ would suggest that its use peritoneally and pleurally might provide an unusually safe local bacteriostatic measure of relatively prolonged effectiveness. For these several reasons it was thought of some interest and possibly of some importance to duplicate the earlier experiments on sulfanilamide and sulfathiazole using sulfaguanidine, and to compare the results of such tests with those obtained with the two former compounds.

EXPERIMENTAL

Mongrel dogs of mixed sexes and weighing 8 to 15 kg. were used as experimental subjects. Prior to experimentation they were deprived of food for about twelve hours, and after administration of the drug, both food and water were withheld for six or seven hours. For the purpose of determining the extent of sulfaguanidine absorption, samples of blood were taken from the saphenous vein at hourly intervals for the first six or seven hours after medication, and then, finally, after twenty-four hours. A sample for control was also taken immediately before experimentation. The blood concentration of sulfaguanidine was determined by a modification of the method described for sulfanilamide by Bratton and Marshall,⁷ using a photoelectric colorimeter with filter No. 540.

When the sulfaguanidine was given orally, it was administered, suspended in water, by means of a stomach tube. For intrapleural and intraperitoneal administration, aseptic surgical procedures were followed, the animal being anesthetized with ether without premedication.

9. Higgins, G. M., and Montgomery, L. G.: Cytology of Peritoneal Fluid in Partially Hepatectomized Animals, *Arch. Path.* 18: 42-49, 1934.
10. Jackson, H. C., and Celler, F. A.: The Use of Sulfanilamide in the Peritoneum, *J. A. M. A.* 118: 194-199, 1942.
11. Key, J. A., and Frankel, C. J.: The Local Use of Sulfanilamide, Sulfapyridine and Sulfamethylthiazole, *Ann. Surg.* 113: 284-293, 1941.
12. Muchella, T. E., and Higgins, G. M.: The Effects of Sulfanilamide, Neoprontosil and Sulfapyridine Upon the Erythrocyte Count of White Rats, *Am. J. M. Sc.* 119: 157-163, 1940.
13. Nakahara, Waro: The Function of Macrophages in Local Resistance to Bacterial Infections, *J. Exper. Med.* 42: 201-214, 1925.
14. Opic, E. L.: Inflammation and Immunity, *J. Immunol.* 17: 329-342, 1929.
15. Rixford, E. L.: Aleuronat Peritonitis: An Experimental Study of Peritoneal and Vascular Reactions, Thesis, University of Minnesota Graduate School, 1933.
16. Seely, S. F., Higgins, G. M., and Mann, F. C.: The Cytologic Response of the Peritoneal Fluid to Certain Substances, *SURGERY* 2: 862-876, 1937.
17. Webb, R. L.: Peritoneal Reactions in the White Rat With Especial Reference to Mast Cells, *Am. J. Anat.* 49: 283-334, 1931.

indicates the statistical significance⁹ of the differences between the rate of absorption from the several surfaces, the least significant differences being noted on comparison of absorption following oral administration with that following peritoneal administration. The values for the blood concentrations after administration orally coincide with those obtained by Marshall, Bratton, White, and Litchfield.³

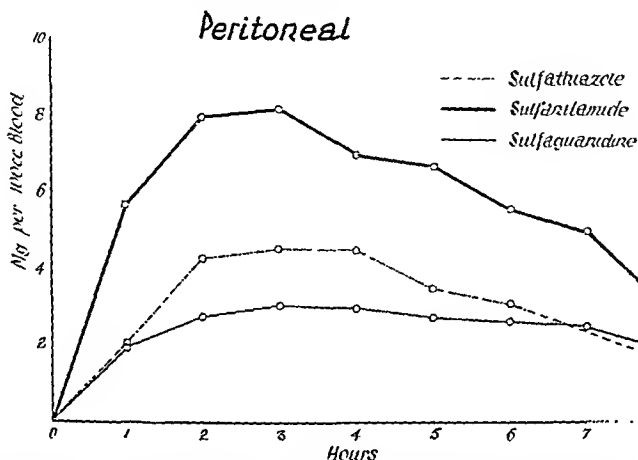


Fig. 2.—Comparative average blood concentrations of sulfaguanidine, sulfanilamide, and sulfathiazole in dogs after peritoneal administration. Five dogs were used for the sulfanilamide, four for the other compounds; the dose of each was 100 mg. per kilogram.

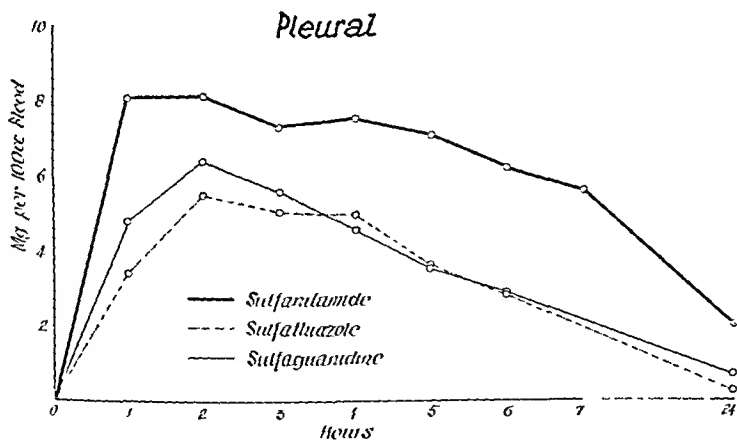


Fig. 3.—Comparative average blood concentrations of sulfaguanidine, sulfanilamide, and sulfathiazole in dogs after pleural administration. Four dogs were used for each compound; the dose of each was 100 mg. per kilogram.

Another small series of experiments was performed to determine approximately the relationship between dose and subsequent blood concentration of the drug. One dog received 200 mg. of sulfaguanidine per kilogram intraperitoneally; the peak blood concentration of 4.88 mg. per 100 c.c. was reached after five hours. Two other dogs similarly received 400 mg. per kilogram. Neither of these latter dogs showed so

The incisions were closed with catgut and silk, and the animals allowed to recover. When the drug was administered into the pleural space, a long incision was made into the fourth right interspace and the powdered sulfaguanidine dusted on the visceral pleura. For intraperitoneal dosage a midline incision was made between the symphysis pubis and the xyphoid of the sternum, the drug being applied to the intestines directly under the greater omentum.

RESULTS

Fig. 1 illustrates the results of our observations when the dose of sulfaguanidine for each of the three methods of administration was 100 mg. per kilogram of body weight, four dogs being used for each method

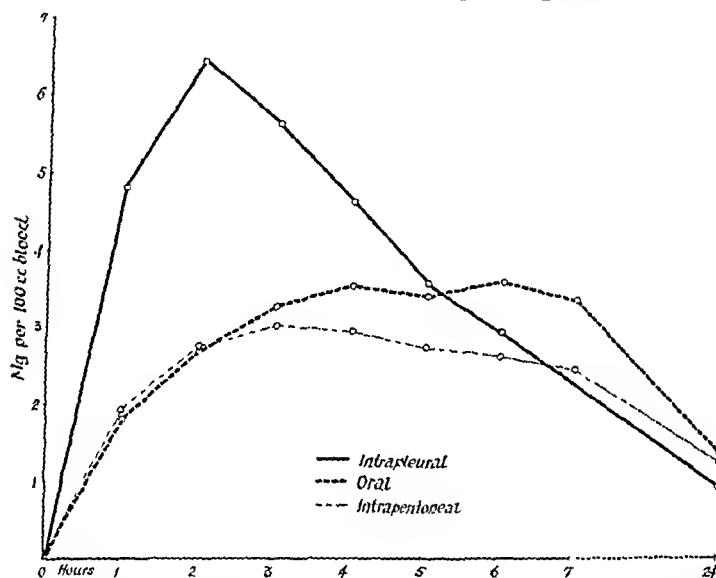


Fig. 1.—Comparative absorption rate of sulfaguanidine in dogs following various routes of administration. Dose of sulfaguanidine, 100 mg. per kilogram.

and the blood concentration values averaged. This is the dose of sulfaguanidine which has been used by oral administration in man.⁸ Table I

TABLE I

T VALUES FOR THE DIFFERENCES IN THE BLOOD CONCENTRATIONS OF SULFAGUANIDINE FOLLOWING DIFFERENT METHODS OF ADMINISTRATION IN DOGS (SIX DEGREES OF FREEDOM THROUGHOUT)

TIME (IN HOURS)	ORALLY/PERITONEALLY	ORALLY/PLEURALLY	PLEURALLY/PERITONEALLY
1	0.43	6.26	6.41
2	0.23	6.26	6.59
3	1.00	3.61	4.00
4	1.90	1.50	5.21
5	1.96	0.07	0.95
6	2.48	1.48	0.66
7	2.53	---	---
24	0.76	2.76	1.70

T values at the 5 per cent point should be 2.447, at the 1 per cent point, 3.707.
For direction of curves refer to Fig. 1.

high a blood concentration as the first one, except after twenty-four hours, when the average blood concentration of these two (2.85 mg. per 100 c.c.) was twice that of the first (1.41 mg. per 100 c.c.). Another dog was given 400 mg. per kilogram orally; the blood concentration of sulfaguanidine never reached the levels noted in the animals receiving only 100 mg. per kilogram. These observations are in keeping with those of Marshall and his associates³ on mice and dogs.

Figs. 2, 3, and 4 show the comparative blood concentrations of sulfanilamide, sulfathiazole, and sulfaguanidine after their administration in identical amounts peritoneally, pleurally, and orally. The values of sulfanilamide and sulfathiazole are those obtained in earlier studies,^{1, 2} performed in a similar fashion as the present ones, with sulfaguanidine. Table II gives the statistical significance of the differences found between the blood levels of the various drugs on administration by the several methods.

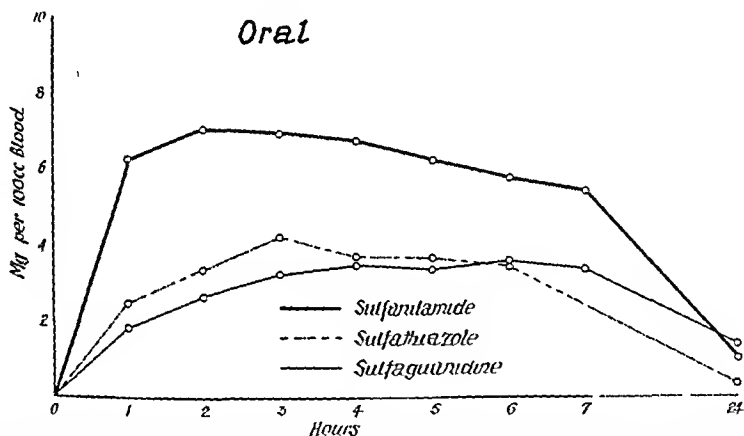


Fig. 4.—Comparative average blood concentrations of sulfaguanidine, sulfanilamide, and sulfathiazole in dogs after oral administration. Four dogs were used for each compound; the dose of each was 100 mg. per kilogram.

DISCUSSION

While sulfaguanidine has been considered as being poorly absorbed from the gastrointestinal tract, the first report on the compound by Marshall and co-workers³ showed that after administration in doses of 100 mg. per kilogram orally to dogs, from 60 to 70 per cent of the chemical could be accounted for in the urine within twenty-four hours; this indicates a degree of absorption and elimination approximately that of sulfathiazole.¹⁰ Low blood concentration values in the case of any drug need not necessarily mean poor absorption, but actually might mean good absorption with rapid elimination. This is what apparently occurs with sulfaguanidine.¹¹ Marshall and his colleagues³ found in dogs that doses of sulfaguanidine larger than 100 mg. per kilogram produced lower blood and urinary excretion levels. We have had similar experiences. Corwin¹² observed that after oral administration to monkeys of sulfa-

TABLE II
T VALUES FOR THE DIFFERENCES IN THE BLOOD CONCENTRATIONS OF SULFAGUANIDINE, SULFANILAMIDE, AND SULFATHIAZOLE
FOLLOWING DIFFERENT METHODS OF ADMINISTRATION IN DOGS*

TIME (IN HOURS)	SULFANILAMIDE/SULFAGUANIDINE			SULFANILAMIDE/SULFATHIAZOLE			SULFATHIAZOLE/SULFAGUANIDINE		
	PERITO- NEALLY*	PLEURALLY	ORALLY	PERITO- NEALLY*	PLEURALLY	ORALLY	PERITO- NEALLY	PLEURALLY	ORALLY
1	4.98	1.74	5.96	4.06	2.52	4.36	0.18	3.27	1.10
2	9.28	2.82	11.00	2.79	4.28	10.00	1.82	1.14	1.43
3	7.32	1.52	12.85	3.34	2.27	3.55	1.98	0.58	1.28
4	4.73	3.59	14.23	2.33	4.81	5.56	1.97	0.61	0.43
5	5.00	4.90	12.90	3.52	4.68	4.68	1.32	0.35	0.58
6	3.97	7.67	4.71	2.85	6.59	2.83	1.21	0.18	0.18
7	3.62	---	3.62	---	---	---	---	---	---
24	0.14	3.08	0.65	0.61	4.42	1.50	1.08	2.64	6.00

*Six degrees of freedom throughout except as asterisked (seven degrees).

T values (six degrees of freedom) at the 5 per cent point should be 2.447; at the 1 per cent point, 3.707.

For direction of curves refer to Figs. 2, 3, and 4.

DRAINAGE OF THE EXTERIORIZED LIVER (EXTERNAL HEPATOSTOMY)

A PALLIATIVE OPERATION FOR JAUNDICE

W. WAYNE BARCOCK, M.D., PHILADELPHIA, PA.

(From the Surgical Department of Temple University)

A WOMAN 68 years old, intensely jaundiced from carcinoma of the biliary tract, was transferred to Temple University Hospital, Nov. 30, 1940, in the hope of obtaining relief from the extreme itching and nausea. No local or general remedy had been palliative, and sedatives and narcotics gave the patient little rest.

Gallstones were removed and a cholecystogastrostomy was done under local anesthesia on Dec. 4, 1940. As the common bile duct seemed fused in a mass of malignant tissue and the gall bladder free from bile, it was not surprising that no improvement followed the operation. Twenty-six days later, under spinal anesthesia, the abdomen was opened again in the hope of finding some outlet for the bile. There were multiple 5 to 7 mm., firm, grayish, metastatic nodules in the liver. One of these was removed for microscopic study by a wedge-shaped resection of the free edge of the right lobe of the liver. Instantly, clear colorless bile poured from a minute duct on the incised surface. The edge of the right lobe, therefore, was exteriorized with four interrupted transfixion sutures of fine alloy steel wire, and the skin and deeper structures closed about the organ with layer interrupted wire sutures. A double suction drain of alloy steel was inserted through a stab wound beneath the liver to evacuate continuously any peritoneal liquids resulting from leakage or exudation. Petrolatum gauze was applied over the exposed liver. Bile, which soon became amber colored, ran from the 1 mm. opening. The jaundice soon cleared and the patient, relieved of the intolerable skin irritation and nausea, was enabled to sleep, to eat, to discontinue using narcotics, and later to leave her room. It was possible to pass a probe to the depth of about 12 cm. into the minute hepatic duct. When an attempt was made to dilate the duct for the insertion of a small cannula, the delicate wall ruptured. The patient returned to her home, January 19. A thin film of epithelium gradually spread over the exposed surface of the liver and the drainage finally ceased, with return of the jaundice and pruritus in March. The patient re-entered the hospital, March 12, 1941, and a thin slice or wedge of the exposed liver was removed painlessly without an anesthetic, opening new ducts. The oozing of blood soon ceased under gauze pressure and the patient was discharged relieved three days later. By April 28, epithelium again had spread over the liver surface and the abdomen had become markedly distended by fluid. A wedge of liver about 8 cm. long, 2 cm. wide, and 2 mm. deep was excised. This was followed immediately by a free flow of bile. Oozing was arrested by light gauze pressure, and a slender, double lumen suction drain for continuous aspiration was inserted into the abdomen under local anesthesia.

The patient died from the progress of the disease about five weeks later. At no time was there suppuration, inflammatory reaction, or

nilamide, sulfathiazole, and sulfaguanidine in doses of 400 mg. per kilogram, sulfaguanidine gave the lowest blood concentrations with sulfathiazole next, and then sulfanilamide. This dose of sulfaguanidine is probably not one to show optimal absorption from the gastrointestinal tract.

Our experiments coincide with more recent experiences that have shown that sulfaguanidine may be rather well absorbed from the gastrointestinal tract.¹¹ The fact that sulfaguanidine is, as a rule, as rapidly absorbed from the gastrointestinal tract, pleural cavity, and peritoneal cavity is in keeping with our previous results obtained with sulfanilamide and sulfathiazole.^{1, 2} The present experiments also suggest that the persistence of bacteriostatic action would be no greater with this substance than with sulfathiazole.

CONCLUSIONS

In normal dogs the rates of absorption of sulfaguanidine in a dose of 100 mg. per kilogram body weight are nearly equal from the gastrointestinal tract and the peritoneal cavity. Absorption from the pleural cavity is definitely more rapid than from either of the other two sites during the first three or four hours after administration.

In similar dosage, sulfanilamide produces generally a significantly higher blood concentration after peritoneal, pleural, and oral administration than either sulfaguanidine or sulfathiazole. The two latter sulfonamides produce more nearly equal blood concentrations. Experimental evidence does not indicate that sulfaguanidine would exhibit a more lasting local bacteriostatic effect than sulfathiazole.

REFERENCES

1. Haag, H. B., Spealman, C. R., and McCue, H. M.: *SURGERY* 10: 572, 1941.
2. Stevens, J. E., Taliaferro, I., and Haag, H. B.: *Proc. Soc. Exper. Biol. & Med.* 48: 223, 1941.
3. Marshall, E. K., Jr., Bratton, A. C., White, H. J., and Litchfield, J. T., Jr.: *Bull. Johns Hopkins Hosp.* 67: 163, 1940.
4. Kent, E. D., and Graham, E. A.: *J. Thoracic Surg.* 11: 198, 1941.
5. Throckmorton, T. D.: *Proc. Staff Meet., Mayo Clin.* 16: 432, 1941.
6. Hawking, F.: *Lancet* 240: 786, 1941.
7. Bratton, A. C., and Marshall, E. K., Jr.: *J. Biol. Chem.* 128: 537, 1939.
8. Stickney, J. M., Heilman, F. R., Barger, J. A., and Dearing, W. H.: *Proc. Staff Meet., Mayo Clin.* 17: 33, 1942.
9. Baten, W. D.: *Elementary Mathematical Statistics*, New York, 1938, John Wiley Sons, Inc., p. 271.
10. Barlow, O. W., cited by Anderson, E. V.: *J. Pediat.* 18: 732, 1941.
11. Piror, W. M., and Poth, E. J.: *Ann. Surg.* 114: 663, 1941.
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evident malignant change of the exposed part of the liver, nor did the skin show irritation from contact with the escaping bile. Through the drainage of bile the progress of the disease became nearly painless and the patient, no longer requiring narcotics, also was relieved of the disturbances resulting from the use of such drugs.

Previous to the above experience, a baby 7 months old, jaundiced from birth and with a greatly enlarged liver, was admitted. Explora-

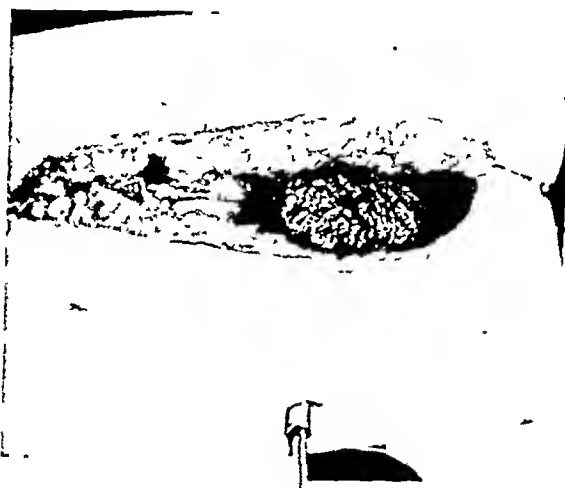


Fig 1—Liver exteriorized in the abdominal wound previous to suture.

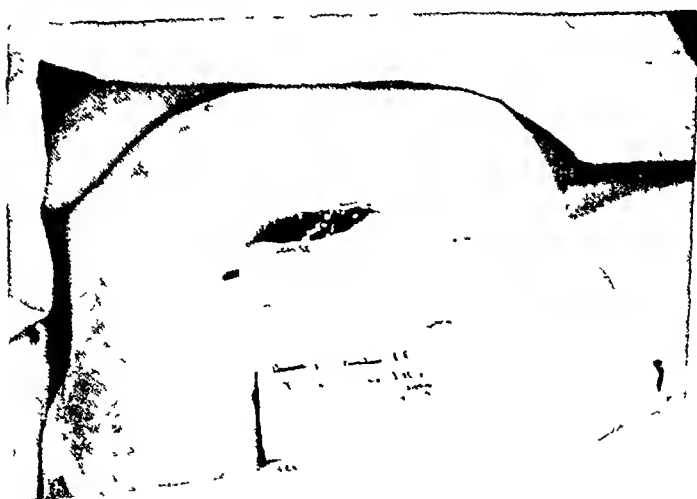


Fig 2—Exteriorized liver, showing flow of bile two and one-half-months after external hepaticostomy.

tory operation, Sept. 15, 1939, showed a large firm liver with very irregular surface. No evidence of gall bladder or of extrahepatic biliary ducts was detected and the condition of the child led me to close the abdomen without attempting to form an anastomotic channel between the liver and the gastrointestinal tract. Not until kodachrome



Fig. 3.—Jaundice and enlarged liver in 7-month-old baby, from agenesis of the extrahepatic biliary system



Fig. 4.—Enlarged liver with greatly dilated bile ducts, shown during operation on the baby.

pictures, taken during the operation, were thrown on a screen was it recognized that the liver surface was covered with greatly dilated bile ducts. In the meantime the child had been returned to his home in a distant town and had died from the progress of the disease. With the subsequent experience, I now, in such a case, would establish a biliary fistula from the surface of the liver in the hope of later anastomosing the fistula with the alimentary tract, either in the manner described previously¹ or in some other way.

SUMMARY

1. A case is presented in which the edge of the liver was exteriorized upon the surface of the abdomen for about five months without unfavorable reaction.

2. The exteriorized liver gradually became covered by a film of squamous epithelium derived from the adjacent skin.

3. From a minute duct opened on the edge of the liver, sufficient drainage of bile occurred to relieve the patient of jaundice and its distressing symptoms.

4. With closure by epithelization of open bile ducts it was possible to obtain additional adequate drainage painlessly and without unfavorable reaction by incision or wedge-shaped resection of the exposed liver.

5. Hepatostomy of the exteriorized liver is suggested as a palliative operation to relieve the patient of intense jaundice and associated symptoms of inoperable malignant disease when other palliative measures are ineffective.

6. Hepatostomy, with or without exteriorization, is suggested as a possible first stage procedure for congenital absence or occlusion of the extrahepatic biliary ducts when a single stage anastomosis to the gastrointestinal tract is unduly hazardous.

REFERENCE

1. Babcock, W. Wayne: A Simple and Effective Method for the Closure of Biliary Fistulas, *Surg., Gynec. & Obst.* 65: 88-90, 1937.

THE SURGICAL APPROACH TO LESIONS OF THE UPPER SCIATIC NERVE AND THE POSTERIOR ASPECT OF THE HIP JOINT

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RECENT experiences with wounds of the sciatic nerve in the gluteal region have emphasized the usefulness of an approach to this region, developed by one of us (H. C. N.). This approach has been found to be of great value in cases of gunshot wound in which numerous pieces of metal are embedded in the area, since it gives a wide exposure facilitating the location and removal of these foreign bodies. Further, it exposes the upper portion of the sciatic nerve well into the sciatic notch, an advantage not obtained by any other approach. Of interest to orthopedic surgeons is the exposure of the posterior aspect of the hip joint afforded by this incision.

The gluteal region and the upper portion of the thigh are widely prepared. As the patient lies prone, the incision is made from just above the posterosuperior spine of the ilium downward and outward in a sweeping curve that passes over the greater trochanter, thence medially to the midline of the thigh and downward for a variable distance (Fig. 1). The skin and superficial fascia are incised along this line, thereby exposing the fascia glutealis which is cut from the trochanter upward and inward to the region of the posterosuperior spine where the gluteus maximus muscle takes its origin. The muscle itself is not incised. The incision is carried downward from the trochanter just lateral to the insertion of the gluteus maximus muscle into the gluteal portion of the fascia lata, to the region of the gluteal sulcus. At this point it may be extended still farther downward along the insertion of the muscle into the linea aspera and then medially through the insertion, or may be carried across the lower fibers of the muscle to the midline of the thigh. The former requires a longer incision, while the latter calls for section of the lower fibers of the muscle. Both have been found satisfactory. Starting at the trochanter, the gluteus maximus muscle with its fascia is separated by blunt dissection from the underlying structures and is turned back like the cover of a book, with nerve and blood supply intact, so that the sciatic nerve lies exposed from the piriformis muscle just below the sciatic notch to the point at which the nerve disappears beneath the long head of the biceps femoris. The gluteus medius, piriformis, gemelli, obturator internus, and quadratus femoris muscles and the upper portion of the long head of the biceps femoris are all within clear view (Fig. 2).

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If the incision is extended down the thigh, the entire sciatic nerve may be exposed from the notch to the popliteal space, the biceps femoris muscle being swung up or down to uncover the mid-portion of the nerve as it passes beneath the muscle. The entire incision is relatively dry, no structure of importance is sectioned, and on closure the parts fall together without tension.

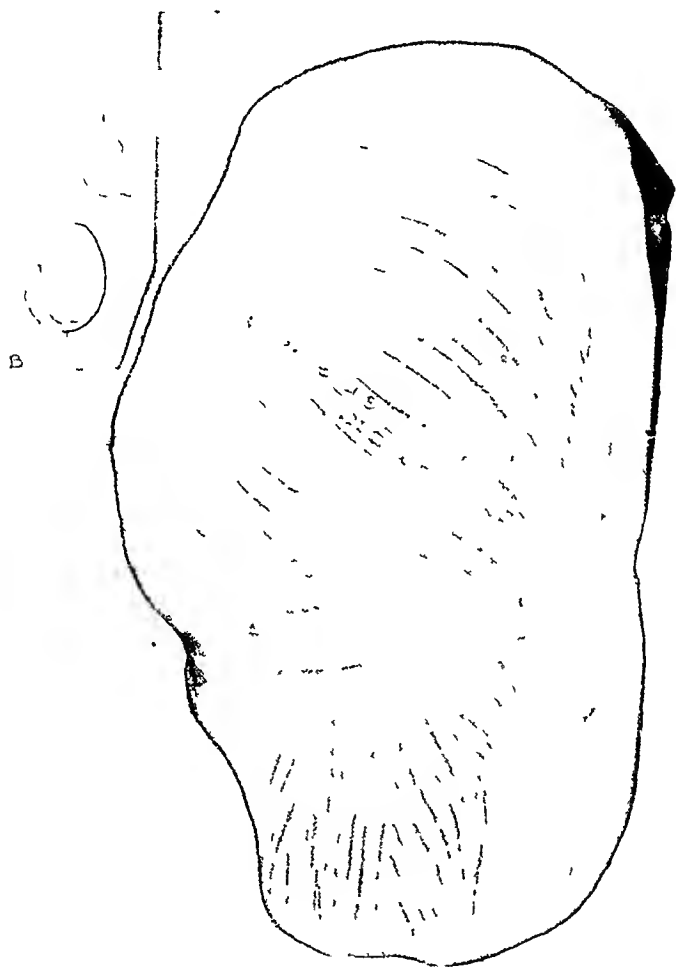


Fig 1—The back of the hip showing A (as if transparent) the attachments of the gluteus and B, the skin incision

A more limited exposure is begun in the same way but is extended only as far as the lower portion of the gluteus maximus muscle. This affords a fairly good exposure of the upper portion of the sciatic nerve and the posterior aspect of the hip joint

ILLUSTRATIVE CASES

CASE 1.—R. M. G. was wounded, Dec 7, 1941, by a piece of bomb case that entered the right gluteal region. His leg jumped straight out and became entirely numb

He noticed no motor weakness. Sensation returned after one week and when he was first examined by us, Jan. 24, 1942, only a small spot over the posterior aspect of the thigh was anesthetic to pin prick. The Achilles and hamstring reflexes were absent. There was slight weakness of the flexor muscles of the thigh, leg, and foot, and these muscles were very tender. There was a great deal of spontaneous pain and cramping. X-ray examination showed a foreign body just below the lesser trochanter, 8.7 cm. beneath the skin at the gluteal sulcus. There was a small scar 3 cm. below and slightly lateral to this. At operation, performed under general anesthesia, the sub-gluteal region was exposed by the method described above. The sciatic nerve was somewhat swollen and harder than normal at a point about 5 cm. below the notch and just below the emergence of the nerve from beneath the piriformis muscle. A hard object was palpated under this muscle and a fragment of a bomb case was removed without difficulty. The scar in the nerve was defined by injecting it with saline solution, causing ballooning of the normal nerve (Fig. 2) and outlining accurately the extent of the scar which occupied the outer one-third of the nerve. Neurolysis was performed. Crystalline sulfanilamide, 4 Gm., was dusted into

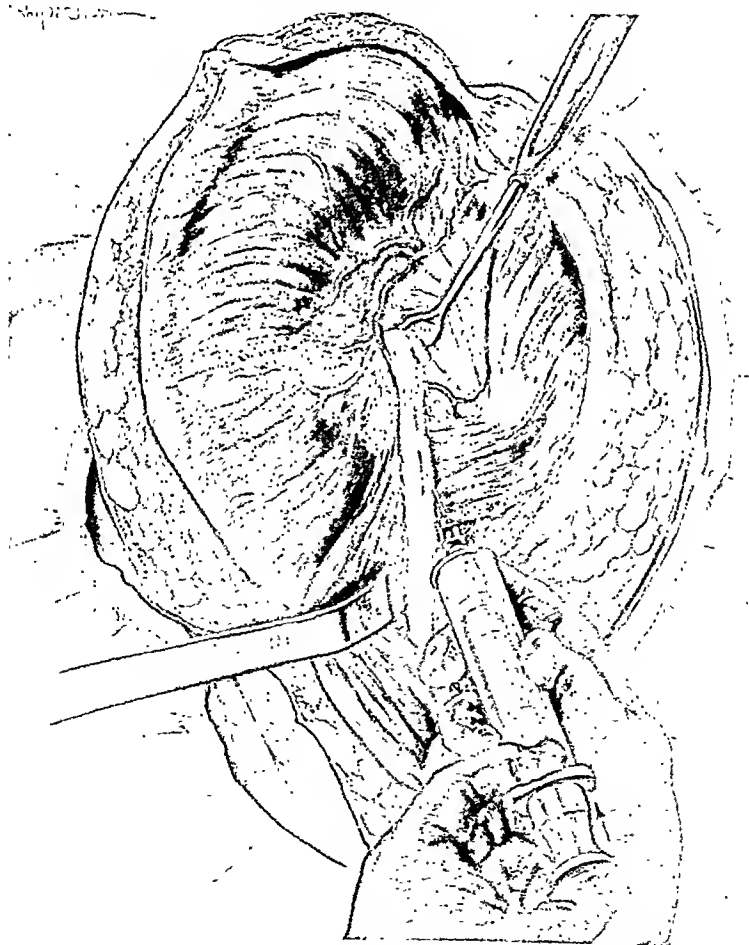


Fig. 2.—The complete exposure with the gluteus maximus turned back showing its nerve and blood supply, the sciatic nerve, the sciatic notch, etc. Note the injection of a scarred nerve with saline solution.

the wound. The cut portion of the gluteus maximus muscle was sutured by several mattress stitches of catgut and the deep fascia closed by interrupted silk sutures. The superficial fascia and skin were closed by interrupted silk sutures with out drainage. The wound healed well, the patient being out of bed on the seventh day, and the sutures were removed on the tenth. The spontaneous pain was completely relieved and the soreness of the muscles was lessened considerably. Some cramping remained but has slowly improved.

On March 21, 1942, the Achilles and lateral hamstring reflexes were still absent but the medial hamstring reflex had returned. No motor weakness was demonstrable. The sensory loss remained unchanged. In short, slight but definite objective and considerable subjective improvement had occurred.

CASE 2.—B. J. H. was struck by machine gun bullets, Dec. 11, 1941. The wound of entrance was in the upper right gluteal region and two fragments had lodged deep in the adductor longus muscle. Numerous metallic fragments were scattered along the line of the projectile which had fractured the acetabulum. The patient was first seen at the Mare Island Naval Hospital on Jan. 2, 1942, complaining of very severe pain which radiated down the back of the right leg to the foot. The Achilles reflex was absent. There was a little sensory loss in the foot over the distribution of the fifth lumbar and first sacral roots. Slight weakness was noted in the muscles of the leg, both anteriorly and posteriorly, and there was some uniform wasting of the leg. The gluteus maximus muscle was completely paralyzed and greatly atrophied. Because of the severe pain, requiring morphine, exploration was decided upon. On Feb. 4, 1942, the incision described above was carried as far as the lower fibers of the gluteus maximus muscle without cutting them. The muscle was reflected and the region of the sciatic nerve exposed. Three fragments of metal were found embedded in scar tissue on top of the nerve and there was a small abscess just medial to the nerve which itself seemed to be intact. The abscess, scar tissue, and metal fragments were removed by blunt dissection. The wound was thoroughly irrigated, crystalline sulfanilamide, 5 Gm., was dusted in, and closure was made with one layer of deep silkworm gut sutures. Cultures from the abscess showed no growth and the wound healed by first intention, the sutures being removed on the tenth day. Following operation the severe pain in the leg and foot was completely relieved and the patient had no complaint referable to the sciatic nerve. At a subsequent operation an abscess in the adductor longus muscle was drained and more metal fragments were removed.

Examination, March 29, 1942, showed that the right Achilles reflex was still absent. The moderate degree of generalized weakness of the leg was unchanged and, as before, included muscles innervated by the femoral as well as the sciatic nerve. Sensation in the first sacral dermatome had returned but that of the fifth lumbar still showed some loss. There was no improvement in the atrophy of the gluteus maximus muscle. The patient had no spontaneous pain but complained when the soleus muscle was squeezed. There was little pain over the nerve and he walked fairly well without support.

SUMMARY AND CONCLUSIONS

A wide exposure of the gluteal and sciatic region is described and illustrative cases are presented. Its advantages are

1. It is quickly and easily opened and closed
2. The exposure of the region is perfect
3. No important structures are sectioned
4. The search for foreign bodies in this area is greatly facilitated and, in point of time, this alone more than compensates for the long incision

POSTOPERATIVE ("ANESTHETIC") PARALYSIS OF THE BRACHIAL PLEXUS

A REVIEW OF THE LITERATURE AND REPORT OF NINE CASES

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PREVENTABLE injuries to the unconscious patient upon the operating table are, fortunately, infrequent though they occur more often than might be suspected; reports of such injuries are likely to be suppressed because of medicolegal complications, and many of the younger surgeons are entirely unaware of the possibility of such an occurrence. Some of those who do know of it have learned by the bitter experience of obtaining a perfect operative result only to have the patient disabled because of mishandling during his period of unconsciousness. In war surgery, when many operations will necessarily be done under great stress, it is imperative to have this complication ever in mind. Foresight on the part of the responsible surgeon may save weeks of disability for men in the armed forces.

Among such preventable injuries, that to the brachial plexus is all too common. Büdinger,¹ of Billroth's clinic, was the first to report such an injury occurring at the operating table, though other surgeons undoubtedly had been fully aware of this complication. Numerous articles were written during the latter part of the nineteenth and the early part of the twentieth century,¹⁻¹⁰ but these serious and wholly preventable injuries have received little consideration recently.¹¹⁻¹³ They are of such discredit to the surgeon, however, that they should be brought more prominently to the attention of the profession.

At first such injuries were attributed to anesthesia itself, but proof was soon forthcoming that they actually result from the patient's position on the operating table, which the surgeon frequently fails to supervise. Furthermore, he may be thinking more of his operative convenience than of a position of comfort for the patient.

The mechanism involved in injuries to the brachial plexus has been the subject of much debate. Büdinger explained such trauma upon the basis of pressure between the clavicle and the first rib; Krumm² believed that the nerves were compressed between the clavicle and the transverse processes of the fifth and sixth cervical vertebrae, and Braun³ thought that the explanation lay in the compression over the head of the humerus while the arm was in external rotation and extension. Further studies seem not to have substantiated these ideas. It seems more logical to assume that injury to the brachial plexus received while the patient is anesthetized may have the same mechanism common to most injuries to the plexus, namely, tension. Gerdy is credited

by French authors with originating the theory of traction, although others mentioned paralysis following a direct pull in the reduction of a dislocated shoulder.^{14, 15} Horsley⁴ emphasized the importance of a spread between the shoulder and the head in the production of these

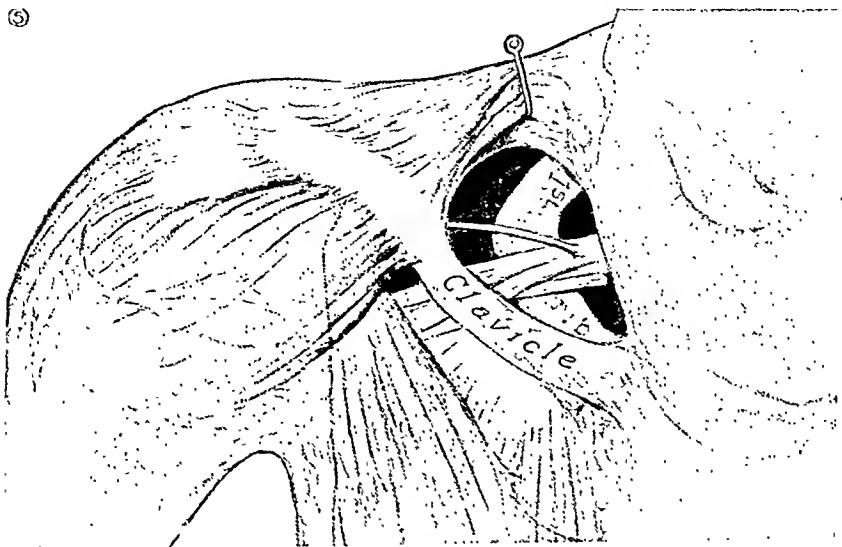


Fig. 1.—Normal anatomy of the brachial plexus in relation to the first rib, clavicle, and pectoralis minor muscle.

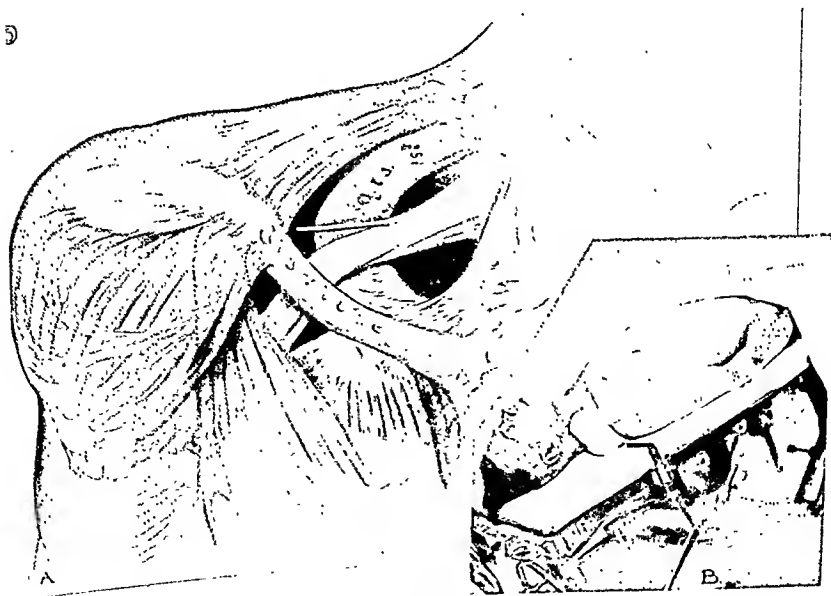


Fig. 2.—A, Anatomic drawing showing the arching of the plexus as it passes over the first rib when the arm is pulled downward in adduction. B, The patient is in the Trendelenburg position, suspended by the arms (the shoulder braces which should take the weight were not properly adjusted) with resultant increased tension as shown in A.

injuries and Stevens¹⁶ agreed with the theory of tension, presenting mechanical evidence in its support.

A number of factors may be contributory. To appreciate all of these, the anatomic relationships of the plexus in relation to the first rib, the clavicle, and the pectoralis minor muscle must be borne in mind (Fig. 1). The injury is essentially one of stretch. Anatomically the nerves are fixed at the transverse processes by invaginations of the prevertebral fascia and in the arm by the axillary fascia. Any structure or structures, whether in a normal or an abnormal position, tending to increase beyond normal limits the distance between the points of fixation of the nerves, will cause injury. The structures involved are listed below.

1. The arch formed by the tendinous attachment of the pectoralis minor to the coracoid process of the scapula acts as a fulcrum in the axilla around which the neurovascular bundle passes. With movements of the shoulder, this arch changes so that the fulcrum is maintained in a neutral position preventing abnormal tension on the nerves. When the arm is pulled downward in adduction the first rib instead of the arch becomes the fulcrum (Fig. 2, A). When the arm is elevated, the scapula rotates and the entire shoulder girdle moves upward so that the fulcrum seeks a level which ordinarily does not interfere with the nerves as they pass into the arm. Should the shoulder be depressed while the arm is in abduction, however, the arch is low and the neurovascular bundle must pass around it to enter the arm (Fig. 3, A).

2. The clavicle also has a place in the consideration of these injuries. When the arm is by the side, the clavicle lies in an oblique lateral position. When the arm is drawn backward, the clavicle assumes a more anteroposterior position and depresses the plexus into the retroclavicular space. If the arm is carried behind the back and drawn downward and across to the opposite side, the radial pulse will disappear. Compression of the subclavian vein by the first rib and the clavicle has been demonstrated by Sampson, Saunders, and Capp.¹⁷ In extreme abduction and extension the clavicle actually compresses the plexus against the first rib (Fig. 4, A), though it is not this compression which causes the injury but rather the increased tension on the nerves distal to the area of compression. In Fig. 4, A, the nerves can be seen to be not only compressed in their proximal course but clearly on tension distally.

3. Lateral deviation and extension of the head have been known to produce injuries to the plexus, particularly when the shoulder is depressed. Horsley demonstrated this emphatically by dropping cadavers so that the impact was sustained with the head in abduction and the shoulder depressed. Frank rupture of the plexus resulted. Obviously, any abduction would tend to increase the distance between the arm and the transverse processes with resultant tension arising from other abnormal conditions.

4. With the arm in external rotation, abduction, and extension, the head of the humerus produces an axillary prominence around which the nerves must pass (Fig. 3, A). This can readily be seen at the time of the axillary dissection during a radical mastectomy. The injury is not produced by pressure on the nerves of the head of the humerus, but indirectly by increasing the distance between the points of fixation.

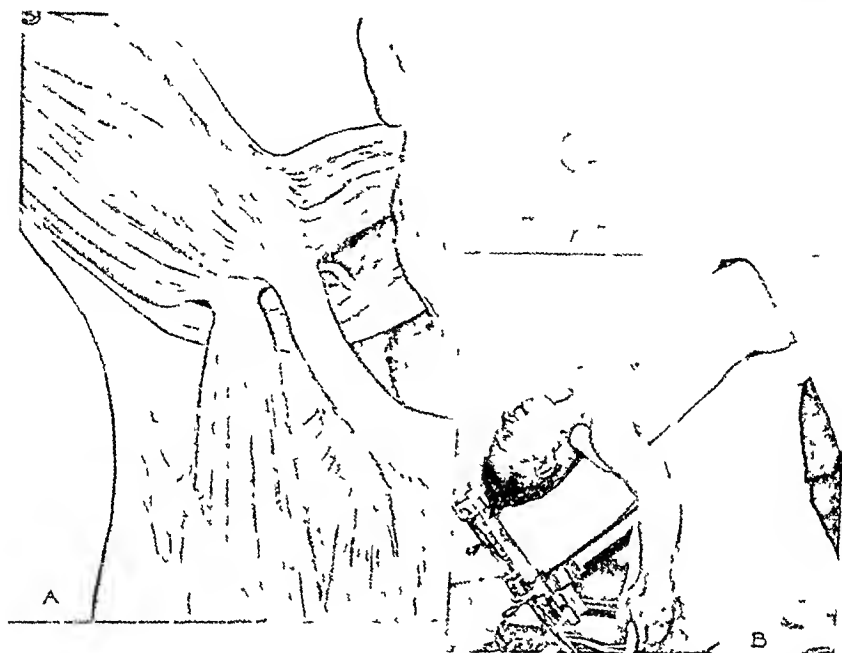


Fig 3—A, Anatomic drawing showing the position of the plexus when the arm is in external rotation abduction and extension the prominence of the head of the humerus and the arch formed by the tendinous process of the pectoralis minor muscle are seen to put the plexus on increased tension B, The patient's arm is in abduction in preparation for intravenous medication the shoulder brace prevents the shoulder from shifting upward consequently the plexus assumes the position shown in 1

5. Several of the foregoing factors are not involved when the arm is drawn downward forcefully. The first rib, however, becomes the fulcrum or prominence over which the nerves pass (Fig 2, A). In those positions in which the clavicle is depressed into the retroclavicular space, the first rib also plays a part in the mechanism of injury by preventing the structures from falling back away from the clavicle, and consequently the plexus may be compressed or at least directed through an S-shaped course.

Injuries to the brachial plexus occurring on the operating table, actually, then, may result from any one of several factors which tend to increase the distance between points of fixation of the nerves, namely (1) the arch formed by the tendinous attachment of the pectoralis minor to the coracoid process, (2) depression of the clavicle into the retroclavicular space, (3) lateral deviation and extension of the head, (4) the prominence formed by the head of the humerus with the arm in external rotation, abduction, and extension, and (5) the first rib.

Congenital anomalies such as the presence of cervical ribs or an anomalous derivation of the plexus may make the nerves more vulnerable. For example, though the plexus is ordinarily derived from the fifth, sixth, seventh, and eighth cervical and first thoracic roots, it may originate at a higher or a lower level, thus, under certain circumstances, placing greater tension on the anomalous roots. Hypertrophy of the scalenus anticus muscle may play a part. These anomalies were not noted in the cases reviewed, nor were they encountered in our own patients.

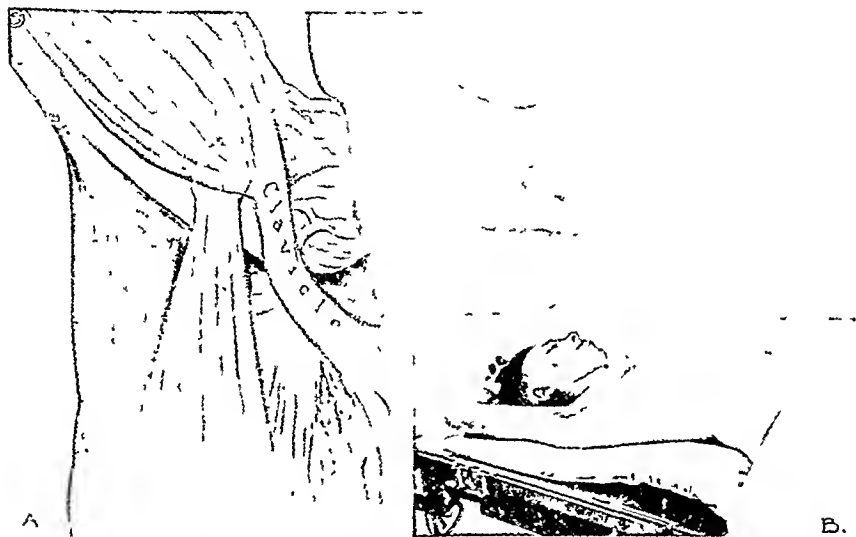


Fig. 4—A, Anatomic drawing showing compression of the plexus by the clavicle against the first rib when the arm is in extreme abduction and extension; injury is caused primarily by tension on the nerves distal to the clavicle and the first rib. B, A patient in this position will show the anatomic features illustrated in A.

During anesthesia, musculotendinous protection is partially or entirely absent. Consequently, there is little resistance to exaggerated positions which result in increased tension upon the plexus as well as the subclavian artery and vein. These positions must be avoided and all movements of the patient must be attended by an adequate personnel.

Pathologic changes are seldom seen. Büdinger¹ made one post-mortem examination but was unable to detect either macroscopic or microscopic changes within the nerves. This has been the experience of surgeons who have examined the plexus at the time of operation following uncomplicated injuries to the plexus associated with traumatic paralysis. There have been, however, reports of ecchymosis, exudate, or sear of the fascial envelopes and fibrous septa in the nerve trunks noted at operation.¹⁸⁻²⁰ Actual rupture is extremely rare even in traumatic cases,²¹⁻²³ and no report was found of such an occurrence in so-called "anesthetic paralysis."

The diagnosis can be made readily if one is aware of the complication, though minor injuries with transient impairment of function may

frequently pass unnoticed. Paralysis, partial or complete, is noted immediately upon awakening. The patient may complain of anesthesia, hyperthesia, hyperesthesia, or paresthesia. In general, sensation seems less affected than motor power, or it may not be involved at all. Reflexes may or may not be present, depending on the severity of the injury. Tenderness in the supraclavicular space usually appears from five to ten days after operation, though local tenderness may be entirely absent. Ecchymosis has not been reported and was not present in this series of patients. Horner's syndrome is occasionally seen, indicating damage to the lower roots of the plexus.

Return of function, fortunately, is usually rapid and complete and sensation, if impaired, returns to normal quickly. An early return of reflexes, if they have been absent, indicates a return of function before active motor power is observed. Some muscular atrophy may result from prolonged inactivity but functional return was noted within one year in all but one of our patients.

Prevention of the injury is the prime consideration. There is no specific treatment for the paralysis. The arm should be placed in splints so that the muscles will be in a neutral position, and physiotherapy should be instituted early. The use of electrostimulation is debatable. Muscular atrophy may occur, depending upon the return of motor power. The patient's confidence must be gained and he must be assured of return of function.

CASE REPORTS

CASE 1.—D. S., 43 years of age, entered the hospital suffering from chronic cholecystitis with cholelithiasis. Her general health was excellent and no history suggestive of a vulnerable peripheral nervous system was elicited. A cholecystectomy was done under nitrous oxide and oxygen induction and ether anesthesia. The patient was in the supine position with the gall bladder lifted in the lower thoracic region. Because the patient was thin and the arms resting on the table interfered with the position of the gallbladder lift, they were placed in abduction and hyperextension behind her head (Fig. 4, B). The procedure lasted two hours and forty minutes. The patient's recovery was uneventful except for paralysis of the brachial plexus, complete on the right and partial on the left. Preservation of function in the long and short flexor muscles of the fingers amounted to 25 per cent and that of the biceps, 10 per cent. Sensation was impaired bilaterally, but was more evident on the right than on the left. Bilateral Horner's syndrome was present. The reflexes were entirely absent except in those muscles partially preserved. There was no supraclavicular tenderness. X-ray examination of the cervical spine showed no abnormalities. Return of sensory function was first noted ten days after operation and was normal in two months. Return of motor function appeared first on the left during the third week after operation and was complete four months later. Return of such function was first noted on the right one month after operation and was complete ten months later except for the loss of extension of the thumb.

The position of choice for the arms is that of flexion over the chest. Damage to the brachial plexus, radial or ulnar nerves would then be impossible. In such a position, however, the elbows may be in proximity to the operative field and furthermore, should an infusion become necessary, some difficulty might be encountered in obtaining a

suitable vein. Consequently, at the University of California Hospital the arms are strapped to the side of the table, with the elbow well padded to prevent compression of the ulnar nerve.

CASE 2.—M. W., 31 years of age, entered the hospital for the correction of retroversion of the uterus and pelvic adhesions. With the use of nitrous oxide and ether anesthesia, dilatation, curettage, Webster suspension of the uterus, and left salpingo oophorectomy were done. The operation lasted two hours and fifty five minutes and the Trendelenburg position was used part of the time. The postoperative course was uneventful except for numbness of the left arm and pain and weakness of the left shoulder. The cords formed by the fifth and sixth cervical roots were the only nerves involved. The paralysis was not complete and hence the reflexes were present. Local examination of the shoulder suggested a tear of the capsule of the joint. X-ray examination of the shoulder and cervical spine showed no abnormalities. Recovery was complete in nine months.

With the wrists strapped to the sides of the table, a sudden change to the Trendelenburg position without proper adjustment of the shoulder braces had resulted in partial suspension of the body by the arm (Fig. 2, B). Since no muscular resistance was present, the tension was transmitted to the fascia and neurovascular structures with resulting injury to the upper roots. The mechanism was that of direct stretch over the first rib. This patient exemplifies the necessity of proper adjustment of the shoulder braces before the Trendelenburg position is assumed.

CASE 3.—H. C., 22 years of age, entered the hospital because of an abscess of the left upper lobe of the lung and chronic empyema on the left. With the use of nitrous oxide and oxygen anesthesia, a partial resection of the fifth and sixth ribs was done. The operation was completed in two hours and thirty minutes. The patient lay on his side with the opposite arm in marked abduction and internal rotation (Fig. 5). This position (the patient lying on his side) may cause lateral displacement of the cervical spine and the marked abduction of the arm causes stretching of the entire plexus. The lateral deviation of the head accounts for the preponderance of stress on the upper cords. Immediately upon awakening, the patient was found to have an incomplete paralysis of the brachial plexus with minimal sensory changes. The entire plexus was involved, but the paralysis of the upper roots, namely the fifth and sixth was complete. There was no supraclavicular tenderness or ecchymosis. Horner's syndrome was not present. No x-ray examinations were made, but there were no findings suggestive of cervical rib. Return of function was first noted on the seventeenth day after operation and was complete seven months later.

CASE 4.—G. E., 35 years of age, had infectious arthritis of the right hip, with ankylosis. An arthroplasty of the right hip was done under avertin in amylene hydrate, and nitrous oxide and oxygen anesthesia. The duration of the operation was three hours and fifty minutes. Her position was similar to that described in Case 3 (Fig. 4, B). Upon awakening she noted a partial paralysis of the brachial plexus involving chiefly the upper two roots. Hyperesthesia was present over the distribution of the fifth and sixth roots. No abnormalities were noted in the x-ray examinations of the shoulder and cervical spine. Within six weeks, sensation was normal and motor power was returning rapidly, six months later no evidence of injury remained.

CASE 5.—C. S., 67 years of age, entered the hospital for repair of a recto-sigmoid stricture. With the use of ether anesthesia a Hemcke-Mikulicz operation requiring four hours' time was performed. During the procedure a venoclysis was given into

the right arm while the patient was in the Trendelenburg position. Immediately after operation she was unable to move her arm. Sensation was unchanged, although at times she complained of pain in the region of the shoulder. Horner's syndrome was present. No cervical ribs were found. Supraclavicular tenderness was present, beginning on the third day. Within twelve hours a return of muscular power was noted and in forty-eight hours function was observed in all muscle groups except those innervated by the fifth and sixth cervical segments. By the thirteenth day after operation, power was present in all muscle groups except the deltoid which showed no evidences of return of function for one month. Pain persisted in the shoulder and was present even eleven months later, at which time there was atrophy and weakness of the deltoid and biceps muscles, though return of function was almost complete.

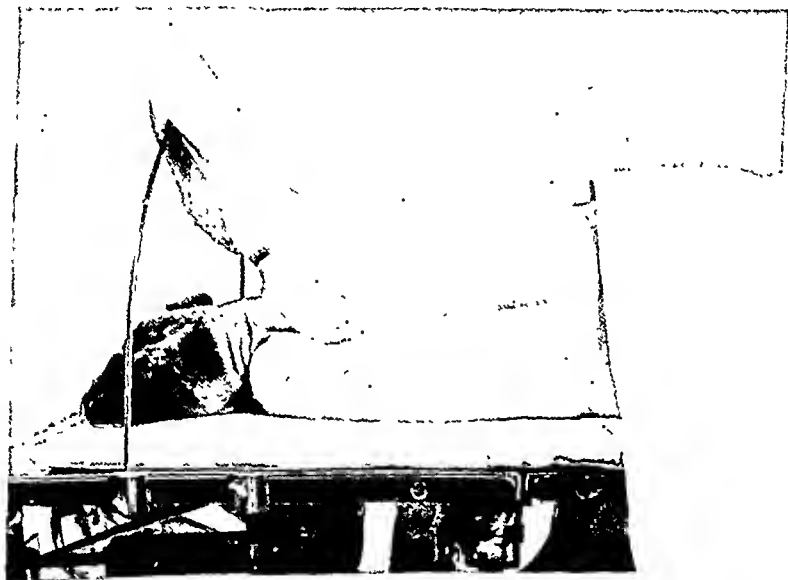


Fig. 5.—Position commonly employed for thoracic procedures, which resulted in injury.

CASE 6.—M. R., 26 years of age, was admitted for a hysterectomy which was done under ether anesthesia. A venoclysis was given into the left arm while the patient was in the Trendelenburg position. Upon awakening, she complained of numbness and inability to use the left arm. All muscles were paralyzed except for 25 per cent function of the flexors and extensors of the fingers. There was hypesthesia over the fifth, sixth, and seventh cervical roots and hyperesthesia of the eighth cervical and first thoracic segments. No Horner's syndrome was present and there was no evidence of cervical ribs. The muscular power returned rapidly so that by the eighth day after operation the biceps and coracobrachialis were the only muscles that had not regained full function. Sensation improved rapidly and was normal ten days after operation. Recovery was complete in two months.

CASE 7.—M. S., 51 years of age, was admitted to the hospital with chronic cholecystitis, cholelithiasis, and probable stones in the common duct. Under ether anesthesia, cholecystectomy and exploration of the common duct were done, the operation lasting two and one-half hours. An intravenous infusion was given into the left arm while the patient was in the Trendelenburg position. Immediately upon awakening she was unable to control her arm and stated that her hand was "still asleep." I first saw her on the third day after operation at which time no sensory findings were detectable. There was no paralysis but a weakness of all

muscles was present, the biceps and flexors of the fingers being most affected. On the twelfth day after operation muscular power had returned except in the biceps; this was normal when the patient was examined six weeks after operation.

CASE 8.—E. B., 53 years of age, was admitted to the hospital for the treatment of a rectal neoplasm. A combined abdominoperineal resection of the lesion was done. A blood transfusion was given into the right arm while the patient was in the Trendelenburg position. When the arm was being brought out in abduction, a clicking sound was heard in the region of the shoulder joint. Immediately after operation, the patient was unable to flex the forearm and the entire arm was numb. No paralysis of the hand and forearm could be made out. X-ray examinations of the shoulder and cervical spine showed no abnormalities. There was a gradual return of function, so that nine months after operation recovery was almost complete.

Cases 5, 6, 7, and 8 illustrate the most common mechanism of injury (Fig. 3, B). The shoulders are depressed and held in that position by the shoulder braces. With abduction of the arm, the entire plexus is put on stretch. The nerves arch over the first rib, pass under the clavicle, which is depressed into the retroclavicular space, as well as under the tendon of the pectoralis minor muscle, and finally around the head of the humerus. When the shoulder is held down by shoulder braces, the upper segments of the plexus will be more vulnerable, while if the shoulder is allowed to move upward, the lower segments will be more affected.

CASE 9.—An obese woman entered the hospital for a pelvic operation which was done with the patient in the Trendelenburg position. The shoulder braces, semi-circular in pattern, were incompletely padded. Injury to the brachial plexus was the result of direct pressure of the brace which became interposed between the clavicle and the first rib.

Baldwin²⁴ reported three similar cases and proposed the use of the "Felter yoke." Shoulder braces must be well padded, adjustable in width as well as in height, and of sufficient depth in order to prevent the occurrence of such injuries.

SUMMARY

1. Nine cases of paralysis of the brachial plexus occurring in anesthetized patients while on the operating table are reported.

2. Unusual positions associated with complete relaxation result in abnormal tension on, and stretch of, the brachial plexus. The anatomic factors involved are shown to be lateral deviation and hyperextension of the head, the first rib, the clavicle, the arch formed by the coracoid process of the scapula and the tendon of the pectoralis minor muscle, and the axillary prominence of the head of the humerus.

3. Certain fundamental principles are emphasized.

- a. With the patient in the Trendelenburg position and the shoulder depressed, the arm should be left at the patient's side.
- b. When the arm is abducted, the head and neck must be held in neutral position or adducted.
- c. The arm should never be abducted beyond ninety degrees under any circumstances.

- d. The arms must not be abducted and extended above the head when the patient is in the supine or the prone position.
 - e. Shoulder braces must be adjusted before the Trendelenburg position is assumed; they should be well padded and adjustable in height as well as in width.
 - f. Wide separation of the head and shoulders must be avoided.
 - g. Movement of an anesthetized patient must be attended by adequate personnel.
4. The possibility of this unfortunate complication must be kept in mind by every member of the operating room staff.

REFERENCES

1. Büdinger, K.: Ueber Lähmungen nach Chloroformmarkosen, *Arch. f. klin. Chir.* 47: 121-145, 1894.
2. Krumm, F.: Ueber Narkosenlähmungen, *Samml. klin. Vortr.*; n. F., No. 139, 1895.
3. Braun, E.: Cited by Garrigues.
4. Horsley, V.: On Injuries to Peripheral Nerves, *Practitioner* 63: 131-144, 1899.
5. Garrigues, H. J.: Anesthesia-Paralysis, *Am. J. M. Sc.* 113: 81-89, 1897.
6. Cotton, F. J., and Allen, S. W.: Brachial Paralysis, Post-Narcotic, *Boston M. & S. J.* 148: 499-502, 1903.
7. Turney, E.: Post-Anesthetic Paralysis, *Clin. J.* 14: 185-191, 1899.
8. McCardie, W. J.: Posture in Relation to General Anesthesia, *Proc. Roy. Soc. Med.* 7: 1 (Sect. Anes.), 39, 1913.
9. Hersman, C. C.: Post-Anesthetic Paralysis, *J. A. M. A.* 36: 231-232, 1901.
10. Green, W. E.: Narcosis Paralysis, With Report of a Case, *Tr. Am. Inst. Homeop.*, 479-481, 1902.
11. Schultze, F.: Bemerkungen über die sogenannte "Narkoselähmung," *Deutsche Ztschr. f. Nervenhe.* 132: 1-3, 1933.
12. Mullen, T. F.: Safeguarding the Unconscious Operative Patient, *West. J. Surg.* 47: 678-686, 1939.
13. Wood, D. A.: Injuries to Nerves During Anesthesia, *California & West. Med.* 53: 267-268, 1940.
14. Malgaigne, J. F.: *Traite des Fractures et des Luxations*, J. B. Ballière et fils, Paris, 1897, p. 55.
15. Flaubert: Memoire sur Plusieurs Cas de Luxation, dans Lesquels les Efforts pour la Réduction ont été Suivis d'Accidens Graves, *Répert. gén. d'anat. et Physiol. Path.* 3: 55-69, 1827.
16. Stevens, J.: Brachial Plexus Paralysis, In: *Codman, E. A.: The Shoulder*, Boston, 1934, T. Todd Co.
17. Sampson, J. J., Saunders, J. B. deC. M., and Capp, C. S.: Compression of the Subclavian Vein by the First Rib and Clavicle, With Special Reference to the Prominence of Chest Veins as a Sign of Collateral Circulation, *Am. Heart J.* 19: 292-315, 1940.
18. Bowlby, A. A.: *Injuries and Diseases of the Nerves and Their Surgical Treatment*, Philadelphia, 1890, P. Blakiston, Son & Co.
19. Sherren, J.: A Series of Cases of Injury to the Peripheral Nerves With Especial Reference to Their Surgical Treatment, *Proc. Roy. Soc. Med.* 2: 1 (Clin. Sect.), 135-144, 1909.
20. Boyer, G. F.: The Complete Histo-pathological Examination of the Nervous System of an Unusual Case of Obstetrical Paralysis Forty-one Years After Birth, and a Review of the Pathology, *Proc. Roy. Soc. Med.* 5: 2 (Sect. Neurol.), 31-56, 1911.
21. Bowlby, A. A.: Injuries of the Nerves, *Lancet* 2: 129-132; 197-200, 1902.
22. Frazier, C. H., and Skillern, P. G.: Supraclavicular Subcutaneous Lesions of the Brachial Plexus not Associated With Skeletal Injuries, *J. A. M. A.* 57: 1957-1963, 1911.
23. Bristow, A. T.: Avulsion of the Brachial Plexus With a Report of Three Cases, *Ann. Surg.* 36: 411-425, 1902.
24. Baldwin, L. G.: The Felter Yoke as a Prophylactic Measure for Postoperative Pressure Paralysis Following the Use of the Trendelenburg Position, *Surg., Gynec. & Obst.* 47: 554-557, 1928.

PLATYBASIA

A REPORT OF A CASE TREATED SURGICALLY WITH IMPROVEMENT

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PLATYBASIA (basilar impression), a rare disease entity even in the special field of neurology, has been slow both of general appreciation and of early recognition. Clinically, this condition is the result of the mechanical and neurological changes produced by a bulging upward of the bony structures about the foramen magnum, as if the bones of the skull in this region were softened and the skull were pushed down on an unyielding cervical spine. A diagnosis of multiple sclerosis, syringomyelia, or one of the various types of spastic paralysis, has often been made. Correct diagnosis in the early stages can probably never be made without the aid of roentgenograms. The present tendency, therefore, to x-ray all cases considered to be multiple sclerosis for a possible platybasia is a practice which should be encouraged.

History.—According to Ebenius,⁴ the first description of platybasia was by Rokitsky in 1844, although DeVet³ mentions a case described in the late eighteenth century. Boogard in 1865,¹ and Virchow in 1877⁷ made detailed clinical studies of the condition, but to Schüller⁶ goes the credit for the first clinical diagnosis by x-ray, in 1911. Platybasia was first brought to the attention of American neurologists by Chamberlain in 1939,² when he reported four cases at the Harvey Cushing Seventieth Birthday Celebration.

Etiology.—The etiology of platybasia, though still obscure, is probably an anomalous development of the basiocciput, and also, frequently, the upper cervical spine. The fact that most cases have an associated partial fusion of the spines of the upper cervical vertebrae gives credence to this theory. Virchow⁷ considered rickets, cretinism, hydrocephalus, idiopathic and puerperal osteomalacia, and senile atrophy as having only incidental etiologic significance. List⁵ believes that not much proof has been offered to support the incrimination of rickets, Paget's disease, or osteomalacia. Trauma, due to repeatedly carrying heavy burdens on the head, is thought significant by Schüller,⁶ who states that the condition is seen more often in countries where this is the practice. Weight-bearing or acute trauma has initiated symptoms or caused exacerbations of symptoms in a number of reported cases including our own.

Diagnosis.—The x-ray is the only certain means of diagnosis in all but far advanced cases. Chamberlain² has proposed the following empirical criterion for diagnosis: A line is drawn on a lateral x-ray film of the skull, from the posterior end of the hard palate to the dorsal

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- d. The arms must not be abducted and extended above the head when the patient is in the supine or the prone position.
 - e. Shoulder braces must be adjusted before the Trendelenburg position is assumed; they should be well padded and adjustable in height as well as in width.
 - f. Wide separation of the head and shoulders must be avoided.
 - g. Movement of an anesthetized patient must be attended by adequate personnel.
4. The possibility of this unfortunate complication must be kept in mind by every member of the operating room staff.

REFERENCES

1. Budinger, K.: Ueber Lahmungen nach Chloroformnarkosen, *Arch. f. klin. Chir.* 47: 121 145, 1894.
2. Krumm, F.: Ueber Narkosenlahmungen, *Samml. klin. Vortr., n. F., No. 139*, 1895.
3. Braun, E.: Cited by Garrigues.⁵
4. Horsley, V.: On Injuries to Peripheral Nerves, *Practitioner* 63: 131 144, 1899.
5. Garrigues, H. J.: Anesthesia Paralysis, *Am. J. M. Sc.* 113: 81 89, 1897.
6. Cotton, F. J., and Allen, S. W.: Brachial Paralysis, Post Nareotic, Boston M. & S. J. 148: 499 502, 1903.
7. Turney, E.: Post Anesthetic Paralysis, *Chn. J.* 14: 185 191, 1899.
8. McCardie, W. J.: Posture in Relation to General Anesthesia, *Proc. Roy. Soc. Med.* 7: 1 (Sect. Anes.), 39, 1913.
9. Heisman, C. C.: Post Anesthetic Paralysis, *J. A. M. A.* 36: 231 232, 1901.
10. Green, W. E.: Nareosis Paralysis, With Report of a Case, *Tr. Am. Inst. Homeop.*, 479 481, 1902.
11. Schultze, F.: Bemerkungen ueber die sogenannte "Narkoselahmung," *Deutsche Zeitschr. f. Nervenhe.* 132: 1 3, 1933.
12. Mullen, T. F.: Safeguarding the Unconscious Operative Patient, *West. J. Surg.* 47: 678 686, 1939.
13. Wood, D. A.: Injuries to Nerves During Anesthesia, *California & West. Med.* 53: 267-268, 1940.
14. Malgaigne, J. F.: *Traite des Fractures et des Luxations*, J. B. Baillière et fils, Paris, 1897, p. 55.
15. Flaubert: Memoire sur Plusieurs Cas de Luxation, dans Lesquels les Efforts pour la Réduction ont été Suivis d'Accidens Graves, *Répert. gén. d'anat. et Physiol. Path.* 3: 55 69, 1827.
16. Stevens, J.: Brachial Plexus Paralysis, In: Codman, E. A.: *The Shoulder*, Boston, 1934, T. Todd Co.
17. Sampson, J. J., Saunders, J. B. deC. M., and Capp, C. S.: Compression of the Subclavian Vein by the First Rib and Clavicle, With Special Reference to the Prominence of Chest Veins as a Sign of Collateral Circulation, *Am. Heart J.* 19: 292 315, 1940.
18. Bowlby, A. A.: *Injuries and Diseases of the Nerves and Their Surgical Treatment*, Philadelphia, 1890, P. Blakiston, Son & Co.
19. Sherren, J.: A Series of Cases of Injury to the Peripheral Nerves With Especial Reference to Their Surgical Treatment, *Proc. Roy. Soc. Med.* 2: 1 (Chn. Sect.), 135 144, 1909.
20. Boyer, G. F.: The Complete Histo pathological Examination of the Nervous System of an Unusual Case of Obstetrical Paralysis Forty one Years After Birth, and a Review of the Pathology, *Proc. Roy. Soc. Med.* 5: 2 (Sect. Neurol.), 31 56, 1911.
21. Bowlby, A. A.: Injuries of the Nerves, *Lancet* 2: 129 132; 197 200, 1902.
22. Frazier, C. H., and Skillern, P. G.: Supraclavicular Subcutaneous Lesions of the Brachial Plexus not Associated With Skeletal Injuries, *J. A. M. A.* 57: 1957 1963, 1911.
23. Bristow, A. T.: Avulsion of the Brachial Plexus With a Report of Three Cases, *Ann. Surg.* 36: 411-425, 1902.
24. Baldwin, L. G.: The Felter Yoke as a Prophylactic Measure for Postoperative Pressure Paralysis Following the Use of the Trendelenburg Position, *Surg., Gynec. & Obst.* 47: 554 557, 1928.

margin of the foramen magnum (Fig. 1). If any of the cervical vertebral elements fall above this line, some degree of platybasia exists.

Chamberlain now considers the presence of an anomalous fusion, or failure of segmentation, at the level of the first cervical vertebra and the occipital segments of the spinal axis (the segments that go to make up the parts of the occipital bone which form the foramen magnum) necessary for the diagnosis of the type of platybasia which produces neurologic signs and symptoms.* The case presented in this paper does not show these anomalies and this viewpoint would, therefore, seem open to question.

A second method is determination of the basal angle, formed by the plane of the clivus and the sphenoidal plane, which runs through the root of the nose and the center of the sella tureica. The extreme limits of the normal range are 110° and 150° as given in the literature.

The neurologic picture of platybasia is partly produced by bony encroachment on the cerebellum within the posterior fossa, due to the upward bulging of the base of the skull. There is also probably some angulation or altered relations of the cerebellar peduncles, and this may be a factor in the production of cerebellar signs. Most of the medullary symptoms are the result of a sharp backward tilting of the axis and atlas, with pressure on the cord by the odontoid process, as the anterior weight-bearing portions of these vertebrae push farther into the cranial cavity than do the posteriorly placed laminae. The clivus is markedly elevated and presses on the pons. These altered relationships all contribute to impairment of posterior cranial and upper spinal nerves.

Because of the varied clinical picture which this condition may present, it is helpful to divide the signs and symptoms into the following groups:

(1) *Cerebellar*: Nystagmus, atonia, clumsiness of the hands, staggering, and unsteady gait.

(2) *Medullary and pontine*: Pyramidal tract symptoms (increased deep reflexes, clonus, absent abdominal reflexes, abnormal plantar responses, and spasticity) and lateral spinothalamic tract impairment (dissociated sensory pain loss).

Tingling, pain, numbness, and weakness of the spastic type may all be produced acutely and often transiently by straining, sudden effort, or trauma.

(3) *Cranial nerve*: Palsies of the posterior group of nerves and those about the petrous ridges.

(4) *Increased intracranial pressure*: Headache, vomiting, choked discs, and blurred vision, from obstruction to cerebrospinal fluid circulation in the posterior fossa.

(5) *Upper cervical peripheral nerves*: Loss of sensibility in the corresponding dermatomes.

*Personal communication to Dr. R. Glen Spurling.

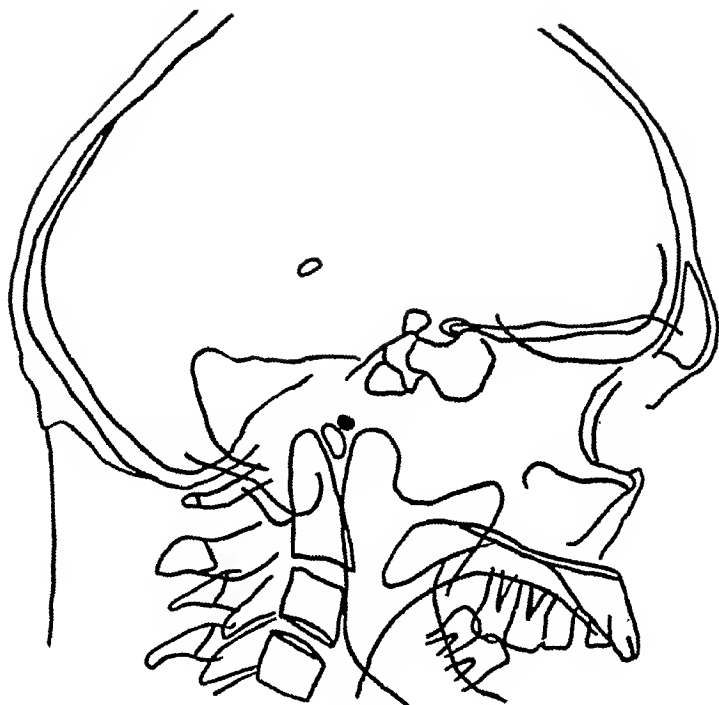


Fig. 1A.



Fig. 1B.

TABLE I—CONT'D

AUTHOR AND CASE NUMBER	PATIENT'S AGE	DURATION OF SYMPTOMS	SYNDROME	OPERATION	RESULTS
VII	24	2 yr.	Cerebello-medullary syndrome	Feb. 7, 1939: Funnel-shaped extension of occipital bone found over cervical dura; Arnold-Chiari malformation. Suboccipital decompression, extensive removal posterior rim of foramen magnum, and laminectomy of C 2 and 3 (C 1 assimilated into occiput); dura incised	Stormy postoperative course with clots removed twice; improved
Walsh, Camp, and Craig ⁵ I	46	22 mo.	Cerebello-medullary syndrome	November, 1940: Arch of atlas absent, C 2 and 3 fused, laminectomy C 2 and 3, posterior rim of foramen magnum removed, dura opened, herniated cerebellar tonsil found; adhesions present between meninges, cerebellum and pons freed	Marked improvement; six months later patient felt normal except slight weakness of left face and tongue
Stevens I	52	29 yr.	Cerebello-medullary syndrome with neck symptoms and upper cervical sensory loss	July 28, 1941: Suboccipital decompression, with laminectomy C 1, 2, and 3	Subjective improvement from first day; regression of neurologic signs continued 3½ mo. later. Patient back at work

(6) *Non-neurologic symptoms:* Neck pain, neck rigidity, torticollis, shortening of the neck, and feeling of weight and pressure in the neck.

From a consideration of these groups of symptoms, it will be seen that early cases, without increased intracranial pressure, and without sufficient bony change to alter the appearance of the neck, can closely simulate multiple sclerosis. Both conditions are usually manifested chiefly by cerebellar, cranial nerve, spastic and sensory signs. Moreover, the essence of the diagnosis of multiple sclerosis, i.e., remission of signs and symptoms, also occurs with platybasia. The mechanism of these remissions can only be surmised.

Therapy.—The resemblance to each other of early platybasia and multiple sclerosis is of major importance when one realizes that active therapy, always the prime consideration from the patient's point of view, is of doubtful value in multiple sclerosis and of definite, though possibly not permanent, value in platybasia. This therapy, undertaken in only eight previously reported cases, consists of removing the bone

TABLE I

RE- CORD	PATIENT'S AGE	DURATION OF SYMPTOMS	SYNDROME	OPERATION	RESULTS
54	21	3 yr.	Increased intra-cranial pressure and cerebellar disturbance	September, 1932: "Suboccipital decompression through bilateral exposure of the cerebellum."	"Some improvement after operation."
	59	6 yr.	Cranial nerve and cerebellar syndrome with shortened neck	November, 1933: "Suboccipital decompression."	"Only slight subjective improvement."
	46	2 yr.	Chiefly cerebellar	September (or October?), 1933: Suboccipital decompression with resection of the arch of the atlas	Subjective improvement followed mild transient pharyngeal paresis
iber- n ²	20	5 yr.	Onset carrying canoe on head. Neck symptoms and medullary compression syndrome, the latter worse after being thrown on buttocks; remission twice after sedatives and lumbar puncture	June 30, 1937: Low occipital craniectomy with laminectomy of C 1, 2, and 3. Dura opened to inspect cord; negative findings	Clinical improvement measurable from the first postoperative day and has continued; entered medical school at age of 22
I	28	17 mo.	Medullary compression syndrome with cerebellum and cranial nerves about petrous ridges involved	Jan. 10, 1938: Low occipital craniotomy and laminectomy at C 1, 2, and 3; dura not opened	Improved markedly postoperatively; well until October, 1938 (9 mo.), when symptoms returned and patient died 15 days after readmission
ist ⁵ I	21	22 mo.	Sudden onset pitching baseball; compression syndrome of medulla	(Laminectomy C 3 and 4 previously done with mistaken diagnosis tuberculosis of spine, in April, 1934.) March 28, 1935: Laminectomy C 1, 2, and 3. Foramen magnum decompressed on the left; bone graft applied occiput to C 5	Postoperative clot removed third day; patient died in few hours after temporary improvement. Postmortem examination showed typical bony changes with compression and softening of medulla

(3) *Cerebrum*: Negative.

(4) *Cerebellum*: Definite swaying on standing with feet together, with a seeming tendency to the right. Well-sustained nystagmus on looking to the right; none on looking to the left. Questionable dysarthria. Some dysmetria in the right arm with right adiadokokinesis.

(5) *Sensory*: Distinct loss of sense of position in both legs.

(6) *Reflexes*: Abdominals markedly diminished bilaterally. Scrotals sluggish. Deep reflexes equal and active. Plantars and confirmatories negative.

(7) Lumbar Puncture revealed initial pressure of 150 mm. of water; negative Queckeustedt; Wassermann and colloidal gold curve negative; cell count 2 per c.c.

A four months' trial on quinine-hydrochloride gave no symptomatic relief.

On Dec. 18, 1937, the patient exhibited spontaneous nystagmus on forward gaze, exaggerated on gaze to the right, and to a lesser degree on left and upward gaze, with some rotary component. He had constant diplopia with displacement chiefly vertical, but no obvious squint.

Caloric tests proved difficult to interpret (arrest of nystagmus when either ear was irrigated with 60 c.c. of cold water, but no dizziness was produced).

The patient walked on a broad base, and could walk tandem for only one or two steps before falling to one side, more often to the left. He was quite awkward at making turns while walking. No dysdiadokokinesis. Reflexes in the arms and legs were normal.

On March 9, 1939, no changes were noted.

X-ray examination of the skull made in July, 1941, showed the base of the skull to be definitely scaphoid in contour and the entire body of the first cervical vertebra and more than one-half of the second to lie above "Chamberlain's line." These changes were considered to be characteristic of platybasia. An axial view showed nothing unusual in the appearance of the foramen magnum.

The patient was admitted to the Norton Memorial Infirmary on July 22, 1941, and the neurologic examination showed the following positive findings:

(1) The patient held his head slightly to the right. Hyperextension of the neck was painful. There was no suboccipital tenderness.

(2) *Cranial Nerves*: Fields and fundi were negative. Nystagmus on right, left, and upward gaze. There was diplopia on gaze in all directions, although there was no obvious strabismus. The patient wore a patch over his right eye, feeling that this eye had more nystagmus than the left when used alone. The other cranial nerves were negative.

(3) *Cerebellum*: There was a suggestion of hypotonia in all the extremities. Rebound phenomenon was present in both arms. There was a mild cerebellar ataxia in the patient's gait, with a tendency to lurch to the right. Finger-to-nose and heel-knee-tibia tests were not ataxic. There was no adiadokokinesis.

(4) *Motor*: Negative.

(5) *Sensory*: There was hypesthesia over the second and third cervical dermatomes bilaterally except the "chin-strap" portion, where overlap probably renders loss imperceptible.

(6) *Reflexes*: Abdominal reflexes on the right were diminished. Cremasteric reflex on the right was not obtained. Other deep and superficial reflexes had a normal threshold and were equal bilaterally. There was no clonus, Hoffman response, or abnormal plantar responses.

Operation.—The operation was performed, July 28, 1941, under procaine infiltration anesthesia, with preliminary medication of nembutal, dilaudid, and hyoscine. The bone about the posterior rim of the foramen magnum was rongeuired away and the laminae of the atlas and the axis were removed. No anomalies of these structures were noted. The dural sac was somewhat angulated as it disappeared beneath the lamina of the third cervical vertebra. Therefore, this lamina

from about the posterior rim of the foramen magnum and performing a laminectomy on the upper two or three cervical vertebrae. This bone removal, not in any way curative, relieves to a great extent the pressure on the cerebellum and posterior cranial nerves, and the angulation and constriction of the medulla at the foramen magnum. As DeVet³ brings out, the bone so removed normally has no weight-bearing function, but with the altered relations in platybasia, the posterior arch of the atlas and posterior margin of the foramen magnum may be weight-bearing. If this is the case, acceleration of the progress of the disease after operation certainly must be considered a possibility.

Previously Reported Cases—The reported cases of platybasia which have been operated upon therapeutically are summarized in Table I.

CASE REPORT

W E W, aged 52 years, salesman by occupation, was admitted to the neurosurgical service of the Norton Memorial Infirmary July 27, 1941 and discharged Aug 11, 1941.

In 1912, at the age of 23 years, the patient, while playing football, forcefully struck the top of his head and experienced a momentary sharp shooting pain in the right ulnar region. It was not like that experienced when one strikes the ulnar nerve at the elbow.

In 1922, at the age of 33, for about a month, he experienced aching and tingling pain in the right hand, arm, shoulder, and upper thoracic spine. The pain in his arm and hand was just like that experienced in the football game in 1912. The ulnar region, beside being painful, was numb. This pain and numbness recurred approximately every two years until 1934, and was present at the time of hospitalization in 1941.

He has been impotent since about 1922, but has never had any sphincter disturbance.

From about 1926 until the present time, he has had double vision, especially on looking to the right. On July 1, 1929, his voice became very husky. For a year this recurred every morning after about thirty minutes of talking to customers, and would continue for the rest of the day. During this period he had a frequent "dry cough" associated with eating. The huskiness decreased in frequency until 1935 when it ceased, but the "dry cough" persisted. When first seen in 1936, he stated that he had had some dysphasia but did not recall this when questioned recently.

Since about 1930, the patient has noticed that hyperextension of his head was painful. His head has been slightly tilted to the right while at rest for the past fifteen or twenty years, he believes. His whole spine has arched to some degree for years. Since approximately 1931, his gait has been drunken in character and he tends to fall to the right. His left leg was "sleepy" for a while in 1930, and again markedly in 1933. Since 1932, he has had tinnitus and deafness in the right ear. He has never noticed any ataxia of his upper extremities.

The first neurologic examination on May 23, 1936, revealed the following positive findings.

- (1) Some suboccipital tenderness on the right.
- (2) Cranial nerves: Nasal side of each disc shows atrophy. III, IV, VI, well sustained nystagmus on looking to the right; none on looking to the left. No rotary motions noted. Paresis of left external rectus and right superior oblique muscles. VIII, Twenty five per cent loss of hearing in the right ear; forth lateralized to the left.

a diagnosis of multiple sclerosis (or syringomyelia, or any other ill-defined degenerative spinal cord disease) should be contacted and investigated for the possibility of platybasia.

The advisability of incising the dura at operation is not agreed upon. Some authors believe that it should be opened in every case to search for anomalies of the nervous structures which might be amenable to surgical therapy. There was no reason to consider seriously the existence of an Arnold-Chiari malformation in this case, as the contour of the dural sac was not abnormal, and the cisterna magna was filled with fluid. The dura was therefore left closed and the nervous structures were thus disturbed as little as possible. The smooth convalescence and continued improvement seem to have justified this course of action in this instance.

SUMMARY

In platybasia the base of the skull about the foramen magnum appears to give way to the forces of gravity, and the unyielding cervical spine invaginates up into the posterior fossa. Pathology is manifested by interference with cerebellar, medullary, cranial nerve, and upper cervical nerve function. Increased intracranial pressure and various symptoms and signs referable to posture and movement of the neck are often present. The etiology, though still unsettled, is probably an anomalous development of the bony structures in the region affected. Platybasia, in its early stages, frequently produces a picture almost identical clinically to multiple sclerosis, even to the occurrence of remissions. X-ray pictures of the skull are necessary for diagnosis of all but far-advanced cases. Surgical therapy has been previously tried in eight reported cases. A ninth case with postoperative improvement is here described in detail.

REFERENCES

1. Boogard, J. A.: Basilar Impression: Its Causes and Consequences, *Nederl. Tijdschr. v. Geneesk.* 2: 81-108, 1865.
2. Chamberlain, W. Edward: Basilar Impression (Platybasia): A Bizarre Developmental Anomaly of the Occipital Bone and Upper Cervical Spine with Striking and Misleading Neurologic Manifestations, *Yale J. Biol. & Med.* 2: 487-496, 1939.
3. DeVet, A.: Basilar Impression of the Skull, *J. Neurol. & Psychiat.* 3: 241-250, 1940.
4. Ebenius, Bertil: The Roentgen Appearance in Four Cases of Basilar Impression, *Acta radiol.* 15: 652-656, 1934.
5. List, C. F.: Neurologic Syndromes Accompanying Developmental Anomalies of Occipital Bone, Axis and Atlas, *Arch. Neurol. & Psychiat.* 45: 577-616, 1941.
6. Schüller, A.: Zur Roentgen-Diagnose der basalen Impression des Schädels, *Wien. med. Wchnschr.* 61: 2593-2599, 1911.
7. Virchow, R.: Beiträge zur physischen Anthropologie der Deutschen, mit besonderer Berücksichtigung der Friesen, Berlin, 1877, F. Dümmler.
8. Walsh, M. N., Camp, J. D., and Craig, W. M.: Basilar Invagination of the Skull (So-Called Platybasia): Report of a Case With Operation, *Proc. Staff Meet., Mayo Clin.* 16: 449-452, 1941.

also was removed. A small nick was made in the dura over the cisterna magna to determine whether or not it was obliterated. It was found to be full of fluid, and so the small hole was closed by placing a muscle stamp over it.

Postoperative Course.—On the third postoperative day the patient stated that his head, throat, and whole body had lost the feeling of "tension" which was present preoperatively. He could cough more easily and his "dry cough" feeling had gone. His body felt "livened up." He had practically lost the numbness in the right ulnar region.

One very interesting bit of history was elicited postoperatively. The patient stated that almost invariably upon arising in the morning he would have to "force his breathing" for about one-half hour. He was conscious of interference with the free automaticity of respiration. His sister, with whom he makes his home, described how she had noticed him taking frequent big deep breaths. This symptom disappeared entirely after the operation.

There was no change in the diplopia.

On the tenth postoperative day the patient stated that extension of his head was much freer and easier. In general, he felt optimistic and pleased with his condition. The neurologic examination however, was essentially unchanged when he was discharged on the fourteenth postoperative day. The following is a quotation from a letter received from the patient on Aug. 22, 1941, three and one-half weeks after operation: "I have been back home a week now and am still feeling fine and gradually picking up a little pep. I can't appreciate too much what you did for me and it looks now like it is not just a dream."

When seen on Nov. 13, 1941, fifteen weeks postoperatively, his status was improved. Diplopia was unchanged, but the nystagmus was less pronounced. He moved his head freely, his coordination was good, and his gait, though he still walked with a broad base, was improving. He has returned to work.

Comment.—In the case herein reported, trauma was the original precipitating factor, as has been noted by other observers. The extent of the role of trauma cannot be fully determined, but it probably acts in conjunction with a pre-existing condition to precipitate the syndrome or to cause an exacerbation of symptoms.

The remission of symptoms, which makes this disease so easily confused with multiple sclerosis, is well demonstrated here. The transient "huskiness" beginning after thirty minutes of talking every morning and lasting the rest of the day continued from 1929 to 1935. There was also some dysphagia during the same period. The huskiness and dysphagia may well have represented daily transient impairment of the vagus nerve after the patient had been in the erect position for a sufficient length of time each morning to allow the changed stresses of gravity to alter relations in the crowded and already strained posterior fossa.

The possibility of a long survival (twenty-nine years) with appreciable symptoms from platybasia is demonstrated. This is a much longer history than those obtained in the other reported treated cases, possibly because most patients with the clinical picture of multiple sclerosis do not continue under the observation of a physician once they have been reconciled to their diagnosis and the ineffectiveness of therapy. If this surmise is valid then every patient who has been dismissed with

and 3,000 units of tetanus antitoxin. Blood transfusions were started. Within an hour the patient's general condition improved somewhat as evidenced by a rise in blood pressure to 100/60 and a fall in pulse rate to 120.

Under ether anesthesia the abdominal wound was reopened and explored. The tangential stab wound had perforated the abdominal cavity and lacerated the splenic flexure of the transverse colon. A profuse hemorrhagic exudate escaped from the peritoneal cavity. The splenic flexure of the transverse colon was mobilized and the bowel exteriorized in the wound and covered over with gauze. A longitudinal incision was made from the groin to the nipple through the middle of the original laceration. The skin and subcutaneous flaps of this cruciate exposure were reflected back. The muscular bellies of the external and internal

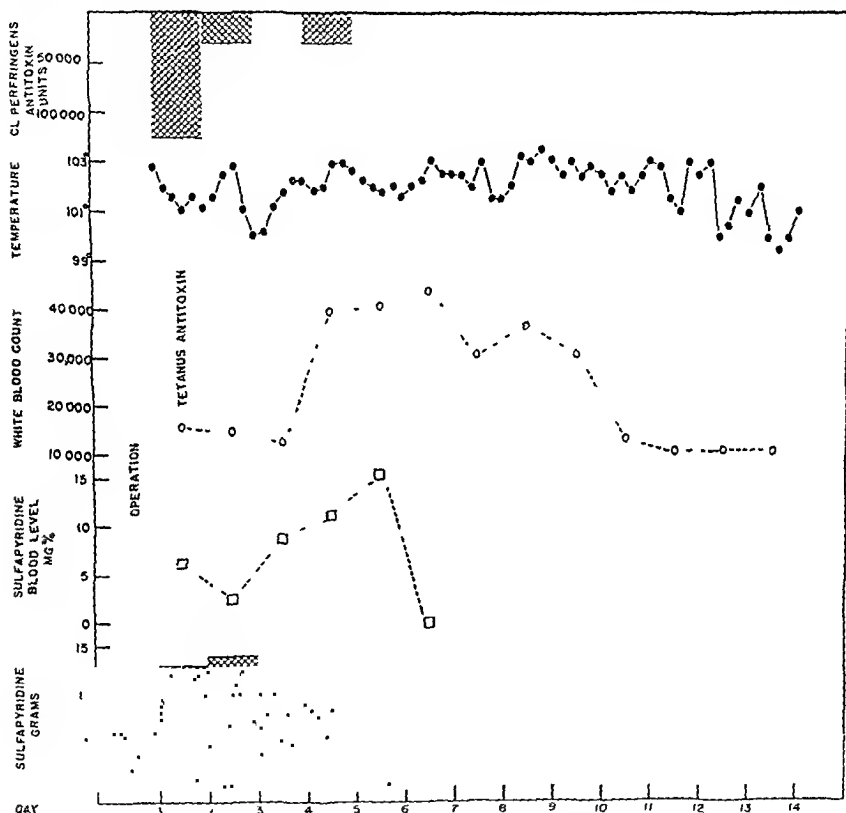


Fig 1—Summary of therapy and clinical course

oblique muscles were crepitant and discolored. These muscles were completely excised from the lumbar aponeurosis to the rectus sheath, and from the groin to the level of the fifth rib. The inferior half of the pectoralis major had to be sacrificed in order to completely remove the underlying attachments of the oblique muscles. The crepitant transversalis muscle was in reality a fibromuscular sheet with very little muscle tissue and was therefore left in place. No attempt was made to expose all areas with obvious crepitus and the scrotum was not opened. This wound was dressed with zinc peroxide and the skin flaps allowed to fall in place. After a complete scrub and change of instruments, the upper right abdomen was entered through a transverse incision. A loop of transverse colon was

PRESERVATION OF THE TRANSVERSALIS MUSCLE IN GAS GANGRENE OF THE TRUNK

CHAMP LYONS, M.D., BOSTON, MASS.
(From the Massachusetts General Hospital)

THE importance of infection of muscular tissue in fatal gas gangrene was emphasized in World War I.¹ Qvist² differentiates the anaerobic cellulitis of nonmuscular tissues from the true gas gangrene with clinical toxemia produced by clostridial infection of muscular tissue. Multiple incisions are effective in the control of anaerobic cellulitis but complete excision of the infected muscle or muscle group is necessary for the control of true gas gangrene. A recent review of gas gangrene of the abdominal wall³ fails to distinguish between anaerobic cellulitis and gas gangrene with muscular infection. It is believed that such a distinction is essential to any plan of treatment and that conservative measures are to be reserved for the management of anaerobic cellulitis.

True gas gangrene of the abdominal wall or trunk constitutes a surgical problem in that excision of the external and internal oblique and transversalis muscles destroys the integrity of the abdominal wall. In the following instance of gas infection of these lateral muscles the truly muscular external and internal oblique muscles were completely removed, but the infected transversalis muscle was left in situ because it was more fibrous than muscular and provided adequate support for the abdominal contents.

CASE REPORT

M. G. H. (Hospital No. 262448), male, aged 31 years, was seen on the evening of Aug. 8, 1940. The patient had suffered a stab wound of the abdomen twenty hours previously. Pain in the abdominal wound developed twelve hours after injury and crepitus was first noted eighteen hours after injury.

Upon examination the patient was moaning with pain, covered with perspiration, and in mild shock with cold, clammy extremities. The blood pressure was 88/40 with a thready pulse of 150. The temperature was 102° F. by rectum. Crepitus was demonstrable from the groin to the nipple, from the spine to the midline of the abdomen, and the scrotum was distended with gas and discolored by a hemorrhagic extravasation. There was a lemon yellow icteric tint to the skin and sclerae. The wound was a transverse laceration of the left upper abdomen, about ten inches long. From the partly separated wound edges there was protruding a large, dark blood clot possessed of a slightly putrid odor.

The patient was removed by ambulance to the Massachusetts General Hospital. Upon entry he was taken directly to an operating room. An intravenous infusion of saline solution was started and the patient received intravenously 6 Gm. of sodium sulfapyridine, 3 therapeutic vials of polyvalent gas gangrene antitoxin,*

*Lederle Laboratories, Inc.
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guinea pigs against intramuscular infection with the strain. (c) Growth in human serum (Nagler⁴) and in egg yolk (MacFarlane⁵) produced opalescence and separation of the lipid element. This reaction was inhibited by specific antitoxin.

Cultural Characteristics.—(a) Morphology: nonmotile, Gram-positive bacillus with no visualized spores; (b) iron milk: stormy fermentation with no blackening; (c) lead acetate and Wilson-Blair plate: blackening; (d) nitrite: positive; (e) indole: negative; (f) iron gelatin: blackened and liquefied; (g) production of acrolein aldehyd from glycerin: positive; (h) violet: negative; (i) sugars fermented: sucrose, lactose, maltose, and dextrose; (j) sugars not fermented: mannite and salicin.

Studies Upon the Patient's Serum (Nagler Reaction).—At no time was it possible to demonstrate a sufficient excess of antitoxin in the patient's serum to inhibit the opalescent change as a consequence of growth of the *Cl. perfringens* in the serum.

COMMENT

A patient was successfully treated for gas bacillus infection of the abdominal wall and peritoneal cavity and true clinical toxemia following a stab wound of the colon. The etiologic organism possessed all the cultural attributes of the *Cl. perfringens* and was toxigenic.

Treatment consisted of local excision of devitalized tissue, defunctioning colostomy, zinc peroxide locally to the wound, sulfapyridine systemically, and antitoxin parenterally.

It is believed that the decision to remove the external and internal oblique muscles and to leave the transversalis muscle contributed to the successful outcome. The transversalis muscle is in reality a thin and fibromuscular structure in many individuals. Since true clinical toxemia is so often dependent upon infection of the muscle with gas bacilli² it would not seem necessary to excise a predominantly fibrous structure. The thinness of the transversalis muscle increases the possibility of successful local treatment when the entire structure is exposed. Hence, it seems reasonable to recommend leaving the transversalis muscle to support the abdominal contents when faced with the problem of gas gangrene of the trunk.

The established gas bacillus peritonitis was promptly controlled by the exteriorization of the lacerated colon and proximal defunctioning colostomy. This is in accord with the established principle that fatal peritonitis from intestinal bacteria is associated with a continued fecal contamination from a faulty suture line or intestinal wound.

The administration of 140,000 units of perfringens antitoxin intravenously did not establish a sufficient circulating excess of antitoxin to inhibit the Nagler reaction. The serotherapy of gas infections is seriously handicapped by lack of data on the required dosage. The Nagler reaction offers a method whereby such dosage may be regulated.

drawn up and severed with the actual cautery between clamps to establish a transverse colostomy and to defunction the left colon. At the conclusion of this procedure the patient's pulse was 110 and the blood pressure was 130/80. He was returned to the ward, transfused again, and given oxygen by the Boothby mask.

Postoperatively he received blood, antitoxin, and sulfapyridine as indicated in Fig. 1. The fever gradually subsided over a period of two weeks but was not entirely normal until the wound was completely epithelialized with the aid of skin grafts two months after entry. The transverse colostomy was closed on Oct. 18, 1940, and the patient was discharged shortly thereafter.

When seen one year after discharge the abdomen appeared as in Fig. 2. There was a hernia in the area of the exteriorized loop of splenic flexure of the colon. An abdominal cosset was worn to protect the area of skin grafting as much as for the support it afforded. He was back at work as a prison guard and in good general health.



Fig. 2—Abdominal scar one year after operation

BACTERIOLOGIC STUDIES

Cultures of the wound and of the peritoneal pus were both positive for the following organisms: (1) *Clostridium perfringens*, (2) *Escherichia coli*, (3) alpha hemolytic streptococcus, (4) two strains of non-pathogenic aerobic Gram-positive sporeforming bacilli (subtilis group). Special studies upon the *Cl. perfringens* included the following:

Toxigenicity.—(a) An overnight culture, 0.2 c.c., in cooked meat medium, killed intramuscularly injected guinea pigs in less than eighteen hours. At autopsy the heart's blood was positive for *Cl. perfringens*. (b) Passive immunization with specific perfringens antitoxin protected

EXTENSIVE, MUTILATING FACIAL DEFECT; COSMETIC CORRECTION WITH LATEX MASK

ADOLPH M. BROWN, M.A., M.D., CHICAGO, ILL.

(From the Department of Otolaryngology, and Laryngology, the University of Illinois College of Medicine)

ONE of the contraindications for plastic surgery as a method to repair facial defects is the presence of coexistent disease. Constitutional diseases like lupus, leprosy, and syphilis, by their devastating and frequently bizarre destruction, often make plastic surgery, as a method of reconstructing missing parts of the body, unwise. The debility which accompanies these diseases, as well as the fact that recurrences may often be expected, makes it difficult to decide upon surgical reconstructive operations for such conditions.

Yet many patients with facial defects caused by consumptive diseases are so disfigured as to create a distinct problem to cover their defects in such a way as to make them socially and esthetically acceptable. Heiser¹ mentions the problem of covering the horrible facial defects in individuals who have leprosy and in whom the disease has been arrested. Many of these patients, he states, remain in the leper colonies even though offered their freedom because they are esthetically unacceptable in their normal social environment.

A case in which extensive destruction of the face has occurred is here presented to demonstrate that a large latex compound prosthesis can be constructed and adapted to conceal unsightly, even open, lesions. It also indicates that a prosthesis of latex may be designed to cover moving parts, with comfort and esthetic satisfaction to the patient.

History.—S. A., aged 29 years, was referred by the department of dermatology, Northwestern University Medical School. His blood Wassermann and Kahn were ++ and he had been treated for several years with antisyphilitic therapy. Destruction of the face was extensive, obliterating the features of the entire face below the eyes. Although several areas on what remained of the face bore weeping ulcers, the patient's condition was more or less quiescent, and although he had been taking his treatments faithfully, he found the treatments did not improve his appearance and he was desperate for some means to disguise his repulsive face.

The patient presented himself wearing a bandage completely covering his face and head with only the ears and eyes exposed. As he unwound his bandage he warned me, saying, "Doctor, my face looks really bad." As illustrated, he exposed a face hideously disfigured. The nose had completely sunk into the nasal cavity, obstructing the airway, the cheeks were gone and were represented only by scar tissue bound down upon the malar bones. The upper and lower lips had disappeared leaving the alveolar ridges and anterior teeth exposed. The skin of the chin and lower jaw was replaced by scar fixed to the mandible. The motion of the mandible was almost completely limited by the scar tissue and by ankylosis of the jaw. The lower eyelids showed mild symptomless ectropion. Saliva drooled over the mandible and could only be controlled with gauze sponges fixed inside the bandages. What remained of his skin was too fragile to permit shaving.

Sulfapyridine was chosen because it was the available sulfonamide of choice in 1940. The zinc peroxide was locally effective against the *Cl. perfringens* but did not prevent troublesome secondary wound infection with *Esch. coli* and *Pseudomonas aeruginosa* (pyocyaneus).

CONCLUSIONS

1. In excising infected muscles for gas gangrene of the trunk it was practical to leave the more fibrous transversalis muscle as a support for the abdominal contents.

2. *Perfringens* antitoxin, 140,000 units, failed to establish a demonstrable excess of antitoxin in the serum.

3. Zinc peroxide was locally effective against the *Cl. perfringens* but did not prevent secondary wound infection with *Esch. coli* and pyocyaneus.

REFERENCES

1. Pathology of Gas Gangrene Following War Wounds, Med. Dept. U. S. Army in World War, 1929 12: 407. U. S. Government Printing Office, Washington, D. C.
2. Qvist, G.: Anaerobic Cellulitis and Gas Gangrene, Brit. M. J. 2: 217, 1941.
3. Quinn, W. C., Lord, J. W., Jr., and Wade, L. J.: Gas Gangrene of the Abdominal Wall, SURGERY 11: 233, 1942.
4. Nagler, F. P. O.: Observations on a Reaction Between the Lethal Toxin of *Cl. Welchii* (Type A) and Human Serum, Brit. J. Exper. Path. 20: 473, 1939.
5. MacFarlane, R. G., Oakley, C. L., and Anderson, C. G.: Haemolysis and the Production of Opalescence in Serum and Lecitho-Vitellin by the Alpha Toxin of *Clostridium Welchii*, J. Path. & Bact. 52: 99, 1941.

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Fig. 1.—Inoperable mutilating deformity caused by malignant syphilis.



Fig. 2.—Profile before prosthesis.

Mentally, the man showed no signs of deterioration, was well oriented as to his position, and very bitter about his plight. He lived in the hospital, never permitted himself to be seen without his bandage, and told me that he had not looked in a mirror for over three years. As a form of self-imposed discipline, he had destroyed all his photographs. Although there is no precedent for a prosthesis so large, we decided to make one.

Technique.—With antisyphilitic precautions, vaseline was applied over the entire face. A negative impression of the entire face was made with molding plaster. The negative impression was removed, soaked in lysol solution for several hours, and while wet, coated thinly with mineral oil. A positive impression of the face was made by pouring a mix of dental stone into the negative impression. The negative was removed, leaving a stone likeness of the face. In order that the prosthesis



Fig. 3.—Prosthesis being applied with gum mastic mucilage.

should be shouldered upon only sounder tissue, the portions of the face which were ulcerated were covered upon the positive cast with additional layers of plaster. This was also done about the lips and teeth to allow for airway, and below the chin to allow for shrinkage of the rubber compound during molding. This space was also necessary to provide a place within the prosthesis for cotton sponges to collect saliva.

Upon the positive cast a new face was sculptured in clay. The features were so constructed as to leave the mouth slightly opened to allow for ventilation. Our aim was to construct a face with regular features but commonplace enough as not to draw attention to the wearer



Fig. 1.—Patient with latex rubber prosthesis. Glasses are worn for esthetic effect; spectacle frame not used for support of mask.



Fig. 5.—Profile with prosthesis; cotton sponges in chin portion collect the saliva.

of the rubber restoration. The lips were modeled with a hint of a smile. The pores of the skin were reproduced by pouring a small mix of fresh plaster over the skin of a normal face. When dry this piece of plaster was used as a tamp to impress the pores and delicate skin tracery into the clay.

The ensemble of the positive cast bearing the clay face was then covered with a fresh batch of dental stone to form two halves of a two-piece mold containing the clay restoration between them. When hardened the two halves of the mold were separated and the clay washed out. The parts were thoroughly dried, reassembled, and were then ready for the molding of the rubber. In order to simulate a shaven skin, electric shaver clippings were thinly spread upon the inner surface of the outer half of the mold. When the mold was poured with precolored latex compound the fine beard shavings thus became imbedded in the visible surface of the prosthesis. This ruse proved quite realistic.

The inside of the superior and posterior edges of the restoration are coated with a gum mastic mueilage when the patient is about to put on his mask. As shown in the photographs, the spectacle frames bearing slightly tinted lenses obscure the feather edge of the prosthesis.

The transformation is astonishing. The patient, after several years of idleness and despair, has now been given a light part-time occupation and is quite happy, even proud, of his prosthesis. The artificial face has made this patient's life enduring.

This work was done under the direction of Dr. Francis Lederer, who first developed flexible translucent prostheses in this country.

REFERENCES

1. Heiser, Victor: *An American Doctor's Odyssey*. New York, 1936, W. W. Norton and Co., Inc., p. 253.
2. Brown, Adolph M.: Latex Compound Prostheses, Notes on Technic, *Arch. Otolaryng.* 35: 720-731, 1942.
3. Brown, Adolph M.: Latex Prosthesis for Cosmetic Restoration of the Amputated Breast, *South. Surgeon* 11: 181-188, 1942.

Editorial

The Questionnaire Method for Standardization

IN RECENT years there has arisen the pernicious habit of sending out questionnaires in order to tabulate many aspects of medical practice. When these are circulated by some individual who wishes to acquire information for a scientific article, a minor evil arises. Such questionnaires are a bother to the colleagues who have to fill them out. As a result, they are always loosely answered, since those who reply to the questionnaire do not have the time to conduct a serious investigation of the problem. Naturally, their time is spent doing their own work rather than doing that of others.

But when the questionnaire involves the standardization of surgical methods we have a much more serious problem. Any scheme of standardization obtained by means of the questionnaire method means that the standard thus obtained will be mediocre for this method compiles the average, not the best, methods. This is beginning to be apparent in more ways than one. If, for example, the sponsors of a recent questionnaire on the standardization of sterilizing technique summarize the usual practice, they will put before the profession the average, not the best, method. Leaders in the profession should not be desirous of standardizing methods at an average level but should push the standards ever higher, up to the highest now known, perhaps even higher, and then try to elevate the institutions up to that high level. This is the only method by which progress can be made.

It appears that standardization through the questionnaire method is but a part of the general threat of the regimentation of people in our country. There seems to be a peculiar lack of personal initiative. There seems to be a desire to conform to the ordinary as opposed to the extraordinary. There seems to be satisfaction with mediocrity as well as the desire for all to walk in the same line and in the same fashion. It may be that the regimentation of our people, as evidenced by what the Government has been trying to do for years, is now exerting its hold on the profession of medicine and we are soon to see standards reduced rather than elevated. It is hoped that the profession will be awake to such destructive ideas and that, at least as regards surgery, we will try to individualize our work at the highest possible peak. If we adopt this attitude, the care of the thousands of young men soon to be our responsibility will be perceptibly bettered.

—*Elliott C. Cutler, M.D.*
Boston, Mass.

Announcements

American College of Surgeons Cancels Clinical Congress

The annual Clinical Congress of the American College of Surgeons which was scheduled to be held in Cleveland, Nov. 17-20, 1942, was cancelled by the Board of Regents of the College at a meeting held in Chicago, Wednesday morning, October 14. Motivated primarily by patriotism, the Regents were influenced by the present conditions surrounding the general war program which have led to a greater burden on the members of the surgical profession in their local communities as a result of the large proportion of the profession which is serving with the armed forces. The Regents by this action took cognizance of the desire of the profession to do nothing which would interfere with the successful prosecution of the war program such as would be caused by temporary absence of its members from civilian duties during the period of the Congress, embarrassment of the transportation system, and interference with the work of the local profession in Cleveland in preparations and presentations incident to such a meeting.

The Activity of the Medical and Surgical Relief Committee of America in the Collection of Medicine and Instruments for Military Purposes

At the recent meeting of the Medical Society of the District of Columbia, held Sept. 29-Oct. 1, 1942, a completely equipped emergency medical field set was donated to Vice Admiral R. R. Waesche of the U. S. Coast Guard by the Medical and Surgical Relief Committee of America, a relief organization with headquarters at 420 Lexington Avenue, New York, N. Y. Ten similar sets have been turned over to the Coast Guard, bringing the total number furnished by the Committee to first-aid posts, emergency medical centers, needy hospitals, and other recognized relief agencies up to 233.

Each of the sets consists of two portable cases completely equipped with instruments, medicines, antiseptics, and a lantern with a set of dry cells to provide power for lights in the event of blackouts or power difficulties. The sets were designed by physicians after a series of experiments during bombing attacks on London.

The campaign to furnish emergency medical field sets is only one phase of the work in which the Committee has been actively engaged since its inception in August, 1940. Organized by Mrs. Millicent Huttleston Rogers and a few New York City physicians to send surplus medicines and surgical instruments to physicians in Great Britain, it has since grown to a nationwide committee consisting of approximately 500 physicians and surgeons assisted by an equal number of professional and non-professional volunteers.

With the spread of war, the organization's scope has broadened to take care of requests from Greece, China, Russia, the Royal Norwegian Forces in Iceland, and the Free French Forces in Northern Africa and Miquelon. Since Pearl Harbor, primary consideration has been given to America's needs.

To date, medical supplies and surgical instruments valued at \$475,690.05 have been sent out by the Committee. The supplies are collected from physicians, hospitals, pharmaceutical houses, and drug stores, then sent to the Committee's New York headquarters. Medicines are sorted and rebottled under the supervision of trained nurses. Instruments are polished, and if necessary, reconditioned. They are then redistributed to organizations where the need for them exists.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE PROBLEM OF THE BLEEDING PEPTIC ULCER

A REVIEW OF 284 PATIENTS ADMITTED TO HARPER HOSPITAL DURING
THE YEARS 1931 TO 1941

M. JORDAN THORSTAD, M.D., DETROIT, MICH.

(From the Harper Hospital)

THE most common complication of peptic ulcers is hemorrhage. Acute massive hemorrhage is manifested by vomiting of blood (hematemesis) or the passage of tarry and bloody stools (melena) together with signs of shock, such as, paleness, weakness, air hunger, dyspnea, collapse, weak and thready pulse, and low blood pressure. The chronic type of hemorrhage is characterized by the presence of tarry stools for many days, resulting in a progressive anemia and subjective symptoms of weakness, vertigo, and malaise.

INCIDENCE

The incidence of hemorrhage as a complication of peptic ulcer is vari-
ously reported in the literature as from 18 to 20 per cent.^{39, 43-45, 84, 102, 104}
This disease is four times as common in the male as in the female.^{18, 20, 43}
The incidence of gross hemorrhage reaches its peak during the fifth
decade and approximately 70 per cent of the cases occur in patients
past the age of 40.^{34, 44} Vital statistics reveal that 70 to 90 per cent of
all deaths from this disease occur in patients over 45 years of
age.^{6, 14, 15, 18, 34} The incidence and mortality rate increase with age
and the presence of arteriosclerosis and hypertension. Many men em-
phasize that approximately 50 per cent of all patients over 45 years of
age who bled from ulcers have had the acute massive type of hemor-
rhage.^{6, 19, 20} Alsted⁷ has found in Denmark that the incidence of
hemorrhage from peptic ulcers has increased but that it is less severe.

ETIOLOGY

Hemorrhage from a peptic ulcer is initiated by many different fac-
tors. From England, Melton⁸¹ has reported a marked increase in the
incidence of bleeding peptic ulcers after the outbreak of the war. He
found that the abnormal increase in mental and physical strain was the
most common etiologic factor. Abuse of the use of alcohol and tobacco,¹⁰⁵
as well as dietary indiscretions, often are the inciting causes. Focal in-
fections,⁹² such as dental caries and abscessed teeth, and infections of
the upper respiratory tract^{34, 88} may cause bleeding from peptic ulcers.

External trauma about the abdomen and unusual physical exertion, particularly heavy lifting,⁹² have been associated with this disease. Vitamin deficiencies, especially vitamin C, developing from the limited diet of the patient suffering from an active peptic ulcer are thought to be an etiologic factor.^{66, 102} Snell¹⁰² also mentions a possible vitamin K deficiency. However, nervous and emotional strains seem to play the major role in provoking hemorrhage from gastric and duodenal ulcers.^{7, 34, 42, 66, 81, 102}

SYMPTOM COMPLEX

The onset and train of symptoms in acute massive hemorrhage are quite characteristic. The patient is often at work when he experiences a sudden sensation of nausea together with a feeling of weakness, unsteadiness, and vertigo, following which he may vomit a variable amount of bright red blood or coffee-ground material. Frequently he collapses and shock is manifested by a cold and clammy skin, paleness, dyspnea, air hunger, and thready rapid pulse. The blood pressure is low and the temperature is often subnormal. Bowel movements are either bloody or tarry in nature. Epigastric distress may or may not be present; if present, vomiting or the taking of an antacid drug will give relief.

PATHOLOGY

Hemorrhage from the upper gastrointestinal tract may occur in the presence of diffuse gastritis, carcinoma of the stomach, rupture of esophageal varices, purpuras and blood dyscrasias, polyposis of the stomach, and most commonly from gastric or duodenal peptic ulcers. Rivers and Wilbur⁹² of the Mayo Clinic found that peptic ulcers were responsible for more than 85 per cent of the cases of hematemesis due to intrinsic gastroduodenal lesions. At operation, and even at autopsy, it may be difficult to discover the source of the hemorrhage if bleeding has stopped temporarily.

Duodenal ulcers are more frequently the source of the hemorrhage than are gastric ulcers.⁹² Hemorrhage from a posterior duodenal ulcer is the most likely to prove fatal. The most severe and persistent type of bleeding results when the pancreaticoduodenal arteries in the posterior wall of the duodenum and the left gastric artery and the gastroepiploic artery in the posterior wall of the stomach are involved. Wilmer,¹⁰⁰ who carefully studied the blood supply of the first part of the duodenum, found that there are two pancreaticoduodenal arcades. Uniting these arcades are large anastomosing vessels running for a long distance on the posteromedial wall of the duodenum. These vessels, in turn, join smaller anastomosing vessels which constitute the very vascular network of arteries which Wilmer calls the *gastroduodenal plexus*. Erosion of one of these larger posterior vessels of this plexus probably causes the acute massive hemorrhage, as compared to the slow chronic hemorrhage due to erosion of the submucosal vessels.

Acute massive hemorrhage from an ulcer usually occurs following an injury to the wall of a small blood vessel. If the vessel is severed transversely, the bleeding end ordinarily retracts and hemorrhage may be only transient. If a section of the wall sloughs out, retraction is difficult and hemorrhage is prolonged. Arteriosclerotic changes in the vessel wall also interfere with retraction of the vessel. In old chronic indurated ulcers, the lack of elasticity of the surrounding tissue prevents the vessel from retracting and hemorrhage is consequently persistent.

DIAGNOSIS

An adequate history, as in all medical conditions, is the most important factor in making a diagnosis of acute massive hemorrhage from a peptic ulcer. A past history of an acute peptic ulcer or indefinite digestive disturbances and the present history of hematemesis or melena together with signs of shock and anemia should always suggest bleeding from a peptic ulcer.

In 1939, Seudder⁵³ introduced a simple and accurate falling-drop method of determining the specific gravity of the blood, which can be carried out at the bedside as frequently as necessary to follow the course of shock. He has shown that in the case of shock from acute massive hemorrhage, there are definite and constant demonstrable changes in the quality of the peripheral capillary blood. The specific gravity falls from a normal value of 1.0566 in males and 1.0533 in females to 1.0400 and less in the presence of severe hemorrhage. The blood hematocrit reading is low and the plasma protein value falls. There is a marked decrease in the whole blood potassium level but an increase in the blood serum potassium level. Moon and associates⁵² demonstrated that the blood coagulation time is shortened in the presence of severe bleeding. The correlation of these values will reveal the severity of the hemorrhage, the progress of the bleeding, and the response to treatment much more quickly and accurately than methods which we have previously had at our disposal. In the early critical stage of massive hemorrhage, the hemoglobin and red blood cell values lag considerably and do not accurately indicate the blood loss.^{57, 54}

Hinton^{54, 55} described a transfusion test for determining the necessity of operation in acute massive hemorrhage as follows. If after two blood transfusions of 500 c.c. each, the hemoglobin and blood pressure remain low, one may assume that a large vessel has been eroded and surgical intervention is indicated.

Barium may be given early by mouth and x-rays taken of the upper gastrointestinal tract as an aid in diagnosis.⁵⁵ The danger in this procedure is not in giving the barium but in the trauma to the viscera by manipulation under the fluoroscope.

The gastroscopic examination of a patient in the presence of acute massive hemorrhage is definitely contraindicated.^{58, 95} Snell¹⁰² reports

its use at the Mayo Clinic in determining the source of hemorrhage in chronic persistent bleeding from the upper gastrointestinal tract.

PROGNOSIS

Patients rarely die during the initial massive hemorrhage from peptic ulcers.^{8, 9, 76, 107} Meulengraet⁷⁷ found that death occurred, on the average, eight days after the onset of the bleeding. Blalock^{21, 22} has found experimentally that death in the presence of severe hemorrhage occurs more often from shock than from exsanguination. It is the opinion of many men that patients with severe bleeding peptic ulcers do not succumb from loss of blood alone, but rather from exhaustion, which is accentuated by the extreme insufficiency of food and drink.^{8, 9, 68, 76, 77, 110, 111}

The mortality rate is extremely high in patients over 45 years of age.^{6, 34, 56} Several authors report that hemorrhage in the female is less serious than in the male.^{25, 26, 31} There is also an abrupt rise in the mortality rate after the second hemorrhage.^{18, 19, 92}

The initial treatment instituted is one of the most important factors determining the prognosis. Many authors report in the literature remarkably low mortality rates with a prompt dietary medical management.

THERAPY

The treatment of acute massive hemorrhage from gastric and duodenal peptic ulcers is a complicated problem. There has been much written during the past decade concerning this phase of the disease. It is agreed that all such patients should be immediately hospitalized and attended by an expert internist and a competent surgeon. The patient should be placed promptly on an adequate dietary medical regime and every effort made within forty-eight hours to single out those cases which require surgical control of the hemorrhage.

The initial shock is combated by rest, quiet, warmth,²⁴ the administration of adrenal cortical extract,⁵⁰ morphine sedation sparingly,⁷⁶ and oxygen.^{100, 112} Transfusions in the presence of active bleeding must be administered with care.

MEDICAL THERAPY

The time-honored medical treatment which had been almost universally accepted and employed until the past decade was the conservative starvation medical management. This regime consisted of a period of starvation of the patient up to several days, administration of large doses of morphine, complete immobilization, infusions of glucose, and transfusions of variable amounts of blood. The period of starvation was followed by the administration of minimal feedings of a bland diet in slowly increasing amounts, as illustrated by a progressive Sippy diet. Close analysis of the mortality statistics reported in the literature for

TABLE I
STARVATION REGIME
MORTALITY STATISTICS AS REPORTED IN LITERATURE

AUTHORS	YEAR	HOSPITAL	TOTAL CASES	DEATHS	MORTALITY (%)
Paterson	1921	London (collected)	1343	52	3.8
Paterson	1924	London (collected)	Acute	massive	11.8
Lynch	1927	Montreal General	31	4	12.9
Ross	1930	Melborne	45	26	58.0
Hinton	1931	Bellerue	52	10	20.0
Mattison	1931	Sweden	---	---	7.0
Bulmer	1932	Birmingham General	467	48	10.7
Chiesman	1932	St. Thomas	191	48	25.0
Allen and Benedict	1933	Massachusetts Gen.	138	20	14.5
Mossberg	1933	Sweden	---	---	9.0
Aitken	1934	London	255	27	11.0
Burger and Hartfall	1934	Guy	117	21	18.0
Christensen	1934	Kommunenhospital	289	23	7.9
Frostad	1934	Norway	---	---	9.4
Hellier and Camb	1934	Leeds	202	26	13.0
Hendon	1935	Louisville	46	5	10.0
Westermann	1935	St. Luke's	50	10	20.0
Babey	1936	Guy	82	4	4.8
Goldman	1937	San Francisco	349	39	11.5
Jankelson and Siegel	1938	Boston City	189	18	9.0
Pfeiffer	1938	Larkenan and Abington Memorial	40	3	7.5
Browne and McHardy	1939	Touro Infirmary	40	4	10.0
Grohn and Lerner	1939	Mount Sinai	94	4	4.2
LaDue	1939	Minneapolis General	82	8	9.8
Marshall and Kiefer	1939	Lahey Clinic	108	5	4.6
Bergh, Hay, Trach	1940	U. of Minnesota Hospital	70	7	10.0
Bergh, Hay, Trach	1940	Collected Cases	2565	262	10.2
Welch and Yunich	1940	Albany	125	11	8.8
Bohrer	1941	Collected Cases	1008	124	11.3
Miller	1941	Collected Cases	5843	508	8.7
Rafsky and Weingarten	1942	Lenox and Beth Israel	271	30	11.0

this type of therapy reveals an astonishingly high mortality rate. The mortality rates, as listed in Table I, range from 4.2 to 58.0 per cent.

In 1906, Lenhartz⁶⁸ described a dietary treatment of 146 patients with bleeding peptic ulcer resulting in a mortality rate of 2.14 per cent. This report did not receive wide acceptance. Andresen,⁸ in 1927, published a report of an entirely new method of management of bleeding peptic ulcers with prompt and fairly liberal feedings of a gelatin-water mixture administered at two-hour intervals. Unfortunately, he reported no statistical data to support the regime. In 1939, he reported a modified Andresen diet as follows: A 1000 calorie diet, consisting of gelatin combined with milk, cream, and glucose flavored with coffee, tea, chocolate, or vanilla, is prepared as a very palatable drink." Six ounces of this formula are given every two hours for the first four days. On the fifth and sixth days egg, cereal, custard, jello, and ice cream are added and on the ninth day a regular modified ulcer diet is begun. At this time Andresen reported a mortality rate of 2.5 per cent for 120 patients with bleeding peptic ulcers treated by this method.

Meulengracht⁷⁶ made a tremendous impression upon the medical profession when he reported, in 1934, a mortality rate of 1.2 per cent for 251 cases of bleeding peptic ulcer treated with a full puree, qualitatively and quantitatively balanced, diet. The original full puree diet as described by Meulengracht is as follows:

- 6:00 A.M. Tea, white bread, and butter
- 9:00 A.M. Oatmeal with milk, white bread and butter
- 1:00 A.M. Dinner of great variety (meat balls, boiled chops, omelet, fish balls, vegetable an gratin, mashed potatoes, tapioca pudding, etc.)
- 3:00 P.M. Cocoa
- 6:00 P.M. White bread, butter, sliced meats, cheese, and tea

This diet is supplemented by the administration of morphine sparingly, iron compounds, and transfusions as indicated. An antacid-antispasmodic mixture is prescribed as follows:

℞
 Sodii Bicarbonatis } āā, gr. XV
 Magnesii Subcarbonatis }
 Extract Hyoseyami gr. LI
 Sig.: One teaspoonful t.i.d.

The patients remain in bed two or three weeks and are discharged, symptom free, in five weeks. They are x-rayed at the end of this period and usually continue on the diet for several months. The chief merit of the Meulengracht diet lay in the reduction of the mortality rate rather than in an ultimate cure of the ulcer.

Mortality statistics reported with the use of the prompt and frequent feeding regime have been collected from the literature and are presented in Table II. The mortality rates are surprisingly low and range from 0.0 to 11.2 per cent. Of interest is the report of Woldman¹¹¹ of a mortality rate of 2.0 per cent employing a continuous intragastric drip of a solution of aluminum hydroxide. This regime was supplemented with two-hour interval feedings of a bland diet. There have been numerous variations of the diet but the Meulengracht and Andresen regimes depend upon the prompt and frequent feeding regardless of the diet. Thus, the type of diet is secondary to the promptness of the administration.

The factors responsible for the excellent results obtained by the immediate feeding regime are as follows:

1. The presence of food in the stomach diminishes the hunger contractions and permits blood clotting to occur in the base of the ulcer. Christensen¹² and Carlson³⁰ have shown conclusively that the fairly well-filled stomach is at all times relatively inactive in contrast to the vigorous activity of the empty stomach.

TABLE II

PROMPT FEEDING REGIME

MORTALITY STATISTICS AS REPORTED IN THE LITERATURE

AUTHORS	YEAR	HOSPITAL	TOTAL CASES	DEATHS	MORTALITY (%)
Lenhartz	1906	Appendorf	146	3	2.14
Howard and Barry	1934	Omaha	12	1	8.3
Alder	1936	Konlonsepitals Aoran	40	0	0.0
Bernstein	1936	Jewish	28	0	0.0
Gubergritz	1936	University of Kiev	15	0	0.0
Giam	1936	Sundby	106	2	2.0
Lincherry and Issos	1937	Birmingham General	38	1	3.6
Witts	1937	St. Bartholomew	24	0	0.0
Boyd and Schlachman	1938	Metropolitan	15	0	0.0
Herlihy	1938	Lewisholm	3	0	0.0
Miller and Elsom	1938	Collected Cases	509	9	1.8
Andresen	1939	Long Island College	120	3	2.5
Barnes	1939	-----	30	0	0.0
Browne and McHardy	1939	Touro Infirmary	37	1	2.7
Chasnoff, Schwartz, and Leibowitz	1939	Beth Israel	21	1	4.8
D'Albana	1939	Long Island College	53	1	1.8
Graham, Kerr, and Alexander	1939	Western Infirmary	44	0	0.0
Jones	1939	St. Bartholomew	50	1	2.0
LaDue	1939	Long Island College	81	--	1.8
Meulengracht	1939	Bispebjerg	491	10	2.0
Crohn and Lerner	1939	Mt. Sinai	23	2	8.6
Vendt	-----	-----	288	7	2.4
Scott	1940	Western Infirmary	60	2	3.3
Allen	1941	Massachusetts Gen.	80	9	11.2
Diers and Voss	1941	-----	57	2	3.5
Emery	1941	Peter Bent Brigham	36	2	5.5
McMillan	1941	Winston-Salem	12	0	0.0
Miller and Nicholson	1941	Univ. of Pennsylvania	32	1	3.0
Miller and Nicholson	1941	Collected in Literature	871		
		Strict Meulengracht	525		3.1
		Bland Diet	133	--	1.5
Mayer and Lightbody	1941	Receiving	---	--	6.0
Schiff	1941	Cincinnati General	60	2	3.3
Scott	1941	Western Infirmary	35	1	3.0
Segal, Scott, and Stevens	1941	Strong Memorial	144	3	2.0
Woldman	1941	St. Luke's	80	2	2.5
Turnbull and Sagi	1939	Evanston			
Rafsky and Weingarten	1942	Lenox, Beth Israel	39	4	10.3
		Meulengracht	34	1	2.9
		Sippy Diet			

2. The presence of food in the stomach increases the tone and the stomach maintains a constant and continuous pressure on its contents. Miller and Nicholson⁸⁰ suggest that this increased intragastric and intraduodenal pressure tends to close an open vessel and promotes clot formation.

3. Gastric secretions are fixed by the foods, preventing the dissolving of the clot.^{8, 12, 26, 32, 76}

4. A high protein diet replaces blood protein lost by the hemorrhage.^{8, 9, 73, 76, 110}

5. A high carbohydrate diet protects the liver and prevents acidosis.^{32, 77}

6. Adequate vitamin C promotes rapid healing of the ulcer and prevents oozing in the posthemorrhagic state.^{77, 88, 90}

7. Regeneration of blood occurs much more rapidly with the administration of food. This was conclusively shown by Schj  dt.⁹⁶

8. The patient's morale is raised and he is calm, composed, comfortable, and cooperative.^{32, 38, 53, 74, 76, 91, 94, 110}

9. The convalescence is shortened.^{74, 76, 77, 97, 110}

Transfusions are an important part of the therapeutic armamentarium. Indications for immediate transfusion are extreme shock, marked air hunger and anoxemia, a hemoglobin level below 40 per cent, and a blood pressure below 90 mm. of mercury. There are reports in the literature both for and against the routine administration of blood early in the presence of severe bleeding, but there is a general tendency toward conservatism. In 1935, Marriott and Kekwicz⁷⁰ proposed the use of massive transfusions as a continuous drip. They have given as much as 3000 to 4000 c.c. of blood over a period of a few days. This is made easier in many hospitals since the advent of the blood bank. Wood,¹¹³ Black and Camb,¹⁷ and Jones,⁶¹ state that slow massive transfusions merely tend to restore gradually the blood pressure to normal level and do not cause increased bleeding. Most reports on the treatment of acute massive hemorrhage advise considerable care in the use of the blood transfusion and suggest that small amounts of 200 to 300 c.c. be administered.^{32, 34, 35, 59, 99} Crohn and Lerner³⁴ feel that the low blood pressure is an excellent natural mechanism for promoting clot formation and should not be unduly disturbed by large transfusions. Shulman and Glass,¹⁰¹ Kilduffe and DeBakey,⁶² and others^{4, 5, 6} hold that blood transfusions exert a hemostatic and coagulative action and that the so-called danger of increasing the blood pressure and "blowing-out" a blood clot is a fallacious belief. Also in this connection Allen⁴ states, "We have seen patients die from the lack of blood but in no instance have we seen transfusions responsible for fatal hemorrhage."

Andresen in discussing the use of an ice bag has this to say,⁹ "As far as the ice bag is concerned, its only advantage, the prevention of undue motion on the part of the patient, in an effort at balancing it on the abdomen, is more than overcome by the disadvantage of wakefulness induced by fear of its being dislodged during sleep."

SURGICAL THERAPY

During the past decade there has been a definite trend among surgeons toward the advocacy of early and radical operative treatment for bleeding peptic ulcers. Finsterer⁴¹ was the first surgeon to advise immediate surgical intervention in acute massive hemorrhage. Working under optimal conditions and operating early, before forty-eight hours had elapsed, he reported a mortality rate of 5.1 per cent in seventy-eight cases. Operating upon seventy-four patients for the same disease after forty-eight hours had elapsed, he obtained a mortality rate of 29.7 per

cent. Therefore, Finsterer advocates early operation, before forty-eight hours have passed, in order to insure a reasonable mortality rate. Gordon-Taylor,^{44, 45} reporting a series of thirty-two patients treated under similar conditions, had a mortality rate of 19 per cent. In a series of 254 operations for bleeding peptic ulcer, not adequately classified as to acute massive hemorrhage or chronic persistent hemorrhage, Walters and Cleveland¹⁰⁵ of the Mayo Clinic reported a mortality rate of 7.4 per cent.

There is a great deal of indecision as to the accepted conditions and indications to be met before surgical intervention is undertaken. Graham,⁴⁷ feels that, given a patient over 50 years of age, who has a hemoglobin level below 50 per cent, operation should be seriously considered. It is generally agreed that patients under 50 years of age have an excellent prognosis for recovery from hemorrhage on a medical management.^{4, 10, 11, 48, 57, 103, 107} Graham⁴⁷ states that a single massive hemorrhage in a young patient is not sufficient justification for operation. Lahey,⁴⁵ Balfour,¹⁰ and Bevan,¹⁶ reserve surgery for those cases of a decisive medical failure or for those with associated complications which in themselves are definite surgical indications.

Rankin and associates⁸⁹ have formulated a group of conditions to be fulfilled before surgery is undertaken. These conditions are as follows: (1) A massive hemorrhage occurring in a known peptic ulcer patient over 50 years of age; (2) a massive hemorrhage occurring in a known peptic ulcer of long standing which has failed to respond to careful continuous medical treatment; (3) a massive hemorrhage following one or more previous episodes of severe bleeding from a peptic ulcer; and (4) when a massive hemorrhage from a known ulcer of long standing or in an arteriosclerotic patient fails to respond to one or more transfusions but shows evidence of continuous or repeated bleeding.

Concerning surgery for bleeding peptic ulcers, Meulengraecht says,⁷⁷ "I consider a mortality rate of 1 or 2 per cent on dietary medical management makes the question unreal to me and relieves me of the responsibility of having to decide in an individual case whether operation is advisable or not." Holman⁵⁶ and Rankin and associates⁸⁹ feel that the routine operative treatment of all bleeding peptic ulcers is impractical and not indicated, but in spite of the excellent results obtained on dietary medical management, there remains a small group of patients in which operative intervention is indicated. Holman^{56, 57} considers the indications for early operation to be (1) an immediate recurrent or persistent bleeding after complete bed rest and (2) a hemorrhage beginning while the patient is receiving adequate medical treatment in the hospital. Wangenstein¹⁰⁷ awaits objective proof that those who attempt the surgical arrest of hemorrhage from a bleeding ulcer are able to perform such procedures with a reasonable mortality.

The mortality statistics for surgical treatment of bleeding peptic ulcers as reported in the literature have been compiled in Table III. In

comparing the mortality rates for surgical treatment with those obtained on adequate dietary medical management, it can be assumed that the safest treatment for the patient in any community, and especially where a competent surgeon is not available, is the prompt dietary medical regime.

The various surgical procedures employed will only be mentioned and not discussed. The operation of choice is partial gastrectomy with removal of the ulcer.^{41, 43, 47, 104, 106, 107, 108} This prevents subsequent hemorrhage which frequently follows other more conservative operations. Other operations which have been advocated are the transduodenal ligation of the eroded vessels, anterior gastroduodenostomy, and excision of the gastric ulcer, with or without gastroenterostomy.

TABLE III
SURGICAL TREATMENT
MORTALITY STATISTICS AS REPORTED IN LITERATURE

AUTHORS	YEAR	HOSPITAL	TOTAL CASES	DEATHS	MORTALITY (%)
Hinton	1931	Bellevue	---	--	20.0
Cullinan and Price	1932	St. Bartholomew	---	--	72.0
Aitken	1934	London	21	7	33.3
Gordon-Taylor	1935	Middlesex	32	6	19.0
Westermann	1935	St. Lukes	42	13	32.5
Hurst and Ryle	1937	New Lodge Clinic	3	3	100.0
Jankelson and Siegel	1938	Boston City	11	3	27.0
Pfeiffer	1938	Larkenau and Abington Memorial	22	5	22.7
Browne and McHardy	1939	Touro Infirmary	14	3	21.4
Crohn and Lerner	1939	Mount Sinai	75	20	26.6
Finsterer	1939	Allgemeines Krankenhaus			
		Before 48 hours	78	4	5.1
		After 48 hours	74	22	29.7
Holman	1940	New York Hospital	45	6	13.0
Bohrer	1941	Knickerbocher and collected cases			
		Gastrectomy	112	20	18.0
		Other operations	48	17	35.4
Miller	1941	Collected cases	383	--	28.0
Walters and Cleveland	1941	Mayo Clinic	254	19	7.4

A REVIEW OF 284 CASES OF BLEEDING PEPTIC ULCER ADMITTED TO
HARPER HOSPITAL, 1931 TO 1941

All cases of bleeding gastric and duodenal peptic ulcers, the acute massive hemorrhage, and the moderately severe hemorrhage, entering Harper Hospital between the years 1931 and 1941 have been reviewed. All patients were classified as having acute massive hemorrhage if they entered the hospital in shock, gave history of hematemesis or melena, had a red blood cell count of three million or less and a hemoglobin level of 50 per cent or less. The statistical data compiled from the charts of these 284 patients admitted with bleeding peptic ulcers is contained in Table IV.

TABLE IV
COMPILED DATA OF 281 CASES BLEEDING PEPTIC ULCER
(HARPER HOSPITAL, 1931 TO 1941)

YEAR	TOTAL CASES	SEX	OVER AGE OF 40 YEARS	CLASSIFICATION		TYPE OF ULCER	PREVIOUS BLEEDING	TREATMENT			CONVALESCENCE (DAYS)	DEATH
				MASSIVE	MILD			STARV.	FEED.	SURG.		
1931	12	3 F. 9 M.	5	8	4	7 Duo. 4 Gast.	9	8	4 Sippy	1	Food 12 Star. 18	0
1932	27	5 F. 22 M.	14	19	8	17 Duo. 8 Gast.	20	20	7 Sippy	4	Food 19 Star. 18	4
1933	19	4 F. 15 M.	11	17	2	7 Duo. 7 Gast.	13	16	3 Sippy	0	Food 13 Star. 14	2
1934	25	2 F. 23 M.	14	16	9	16 Duo. 5 Gast.	18	15	10 Sippy	3	Food 9 Star. 16	2
1935	18	4 F. 14 M.	15	15	3	10 Duo. 5 Gast.	14	13	5 Sippy	1	Food 13 Star. 16	4
1936	16	4 F. 12 M.	11	12	4	7 Duo. 8 Gast.	14	11	5 Sippy	0	Food 15 Star. 14	2
1937	30	9 F. 21 M.	18	25	5	17 Duo. 18 Gast.	21	23	5 Sippy 2 Meul.	1	Food 8 Star. 15	4
1938	13	1 F. 12 M.	9	10	3	8 Duo. 3 Gast.	12	9	4 Sippy	1	Food 17 Star. 10	1
1939	37	7 F. 30 M.	30	31	6	24 Duo. 11 Gast.	22	23	11 Sippy 3 Meul.	1	Food 15 Star. 18	1
1940	41	6 F. 35 M.	32	25	16	30 Duo. 10 Gast.	34	17	21 Sippy 3 Meul.	1	Food 16 Star. 16	0
1941	46	9 F. 37 M.	30	30	16	31 Duo. 11 Gast.	30	25	12 Sippy 9 Meul.	3	Food 14 Star. 17	2
Total	284	54 F. 230 M.	189	208	76	173 Duo. 90 Gast.	207	180	104	76	Food 14 Star. 16	22

There were 208 patients who suffered from acute massive hemorrhage and 74 patients who had mild or chronic bleeding from either gastric or duodenal peptic ulcers. The distribution of the 208 cases is shown graphically in Fig. 1. There were seventy cases of acute massive hemorrhage treated by a prompt and frequent feeding regime. Eleven patients received the Meulengracht diet and the remainder received the Sippy fluid diet or a soft diet. There were 138 patients treated by the strict starvation regime. Seven patients with acute massive hemorrhage were operated upon with one death.

During the eleven-year period, 1931 to 1941, there were twenty-two deaths from bleeding gastric and duodenal peptic ulcers treated at Harper Hospital. One death was due to surgery; a pyloroplasty was performed and a fatal peritonitis developed. There were twenty-one deaths in those patients treated medically. These deaths are analyzed in Table V.

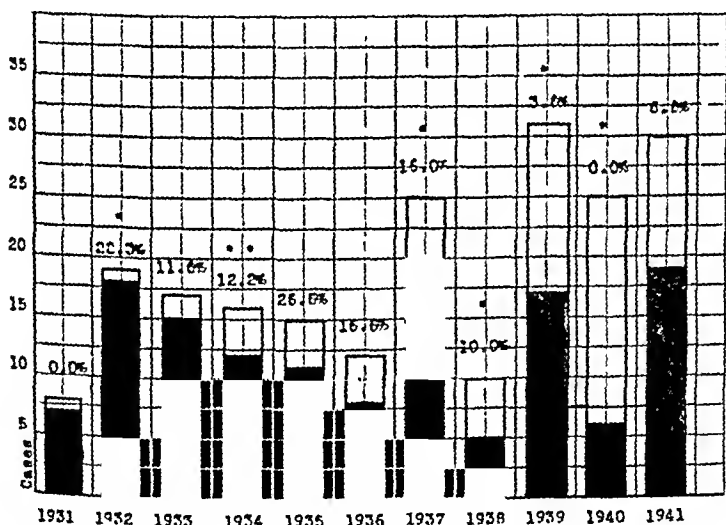


Fig. 1.—Distribution of 208 cases of acute massive hemorrhage.

Cases treated by prompt feeding (70 patients).

Cases treated by starvation regime (138 patients).

Indicates each patient treated surgically (7 patients).

%

Mortality rate yearly on medical management.

After reviewing the data as compiled in the last three tables, the following conclusions can be drawn.

1. There were twenty-one deaths in the entire series of 284 cases of bleeding peptic ulcers. All deaths occurred in the presence of acute massive hemorrhage. The mortality rate for the 208 cases of acute massive hemorrhage was 10.0 per cent.

2. Seven patients with acute massive hemorrhage were submitted to surgery. There was one death, resulting in a surgical mortality rate

TABLE IV
COMPILED DATA OF 284 CASES BREEDING PEPTIC ULCER
(HARPER HOSPITAL, 1931 TO 1941)

YEAR	TOTAL CASES	SEX	AGE OF 40 YEARS	CLASSIFICATION		TYPE OF ULCER	PREVIOUS BLEEDING	TREATMENT			CONVALESCENCE (DAYS)	DEATH
				MASSIVE	MILD			STARV.	FEED.	SURG.		
1931	12	3 F. 9 M.	5	8	4	7 Duo. 4 Gast.	9	8	4 Sippy	1	Food 12 Star. 18	0
1932	27	5 F. 22 M.	14	19	8	17 Duo. 8 Gast.	20	20	7 Sippy	1	Food 19 Star. 18	4
1933	19	4 F. 15 M.	11	17	2	7 Duo. 7 Gast.	13	16	3 Sippy	0	Food 13 Star. 11	2
1934	23	2 F. 21 M.	14	16	9	16 Duo. 5 Gast.	18	15	10 Sippy	3	Food 9 Star. 16	2
1935	18	4 F. 14 M.	15	13	3	10 Duo. 5 Gast.	11	13	3 Sippy	1	Food 18 Star. 16	4
1936	16	4 F. 12 M.	11	12	4	7 Duo. 8 Gast.	11	11	3 Sippy	0	Food 15 Star. 14	2
1937	30	9 F. 21 M.	18	25	5	17 Duo. 18 Gast.	21	23	3 Sippy 2 Meul.	1	Food 8 Star. 15	4
1938	13	1 F. 12 M.	9	10	3	8 Duo. 3 Gast.	12	9	4 Sippy	1	Food 17 Star. 10	1
1939	37	7 F. 30 M.	30	31	6	24 Duo. 11 Gast.	22	23	11 Sippy 3 Meul.	1	Food 15 Star. 18	1
1940	41	6 F. 35 M.	32	25	16	30 Duo. 10 Gast.	34	17	21 Sippy 3 Meul.	1	Food 16 Star. 16	0
1941	46	9 F. 37 M.	30	30	16	31 Duo. 11 Gast.	30	25	12 Sippy 9 Meul.	3	Food 14 Star. 17	2
Total	284	34 F. 250 M.	189	208	76	173 Duo 90 Gast	207	180	101	16	Food 14 Star. 16	22

evening and was not fed until the next morning. However, the two deaths gave a mortality rate of 2.8 per cent on immediate feeding management.

4. Nineteen deaths occurred in a series of 138 patients with acute massive hemorrhage treated by a starvation regime, resulting in a mortality rate of 13.7 per cent.

5. Seventeen deaths occurred in patients over 45 years of age, an 80 per cent incidence.

6. There were no deaths from the initial massive hemorrhage. Eighteen patients who expired from acute massive hemorrhage gave no history of previous episodes of bleeding; conversely, only three patients who died gave a history of previous bleeding.

7. The average period of hospitalization of the fatal cases was from six to ten days, corresponding with the figure reported by Meulengracht.⁷⁶

8. This condition is four times as common in the male as in the female. However, there were seven deaths in the group of 54 female patients with acute massive hemorrhage, giving a mortality rate of 13.0 per cent. Fifteen men died in the group of 230 male patients. The mortality rate for men is 6.5 per cent, much less than for women.

9. Duodenal ulcers are more often the source of the hemorrhage than are gastric ulcers. The mortality rate is higher for acute hemorrhage from gastric peptic ulcers than for duodenal peptic ulcers.

10. There has been a marked increase in the number of patients with acute massive hemorrhage from peptic ulcers admitted to Harper Hospital during the past three years.

11. The trend in treatment for acute massive hemorrhage from peptic ulcer at Harper Hospital is definitely in favor of the prompt and frequent feeding management.

SUMMARY

In acute massive hemorrhage from gastric and duodenal peptic ulcers, the mortality rate is markedly lowered by the prompt and frequent administration of an adequate dietary medical regime.

Of 284 patients admitted to Harper Hospital from 1931 to 1941 with the diagnosis of bleeding peptic ulcer, there were 208 patients with acute massive hemorrhage.

The mortality rate for seventy patients with acute massive hemorrhage treated by a prompt and frequent feeding regime was 2.8 per cent.

The mortality rate for 138 patients with acute massive hemorrhage from peptic ulcer treated by a starvation regime was 13.7 per cent.

TABLE V

ANALYSIS OF 22 DEATHS FROM ACUTE MASSIVE HEMORRHAGE
HARPER HOSPITAL (1931 TO 1941)

YEAR	AGE	SEX	TYPE OF ULCER	BLEEDING	CAUSE OF DEATH	TREATMENT	HOSPITALIZATION PERIOD
1932	48	F.	Duo.	?	Acute Massive Hem.	Starvation Diet	6 Days
1932	50	M.	?	Primary	Acute Massive Hem.	Starvation Diet	11 Days
1932	58	M.	Duo.	Primary	Acute Massive Hem.	Starvation Diet	5 Days
1932	38	M.	?	Primary	Acute Massive Hem.	Starvation Diet	11 Days
1933	70	M.	Duo.	Secondary	Acute Massive Hem.	Starvation Diet	1 Day
1933	49	M.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	11 Days
1934	34	M.	Duo.	Primary	Acute Massive Hem.	Starvation Diet	13 Days
1934	31	M.	Duo.	Secondary	Pyloroplasty with peritonitis	Starvation Diet	17 Days
1935	50	M.	Duo.	Primary	Acute Massive Hem.	Sippy Diet	20 Days
1935	46	M.	Duo.	Primary	Acute Massive Hem.	Starvation Diet	6 Days
1935	52	M.	?	Primary	Acute Massive Hem.	Starvation Diet	3 Days
1935	56	F.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	26 Days
1936	59	F.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	4 Days
1936	52	M.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	6 Days
1937	31	F.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	5 Days
1937	64	F.	?	Primary	Acute Massive Hem.	Starvation Diet	1 Day
1937	40	M.	Gast.	Secondary	Acute Massive Hem.	Starvation Diet	59 Days
1937	47	F.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	8 Days
1938	50	M.	Duo.	Primary	Acute Massive Hem.	Soft Diet (few feedings)	4 Days
1939	62	M.	Gast.	Primary	Acute Massive Hem.	Starvation Diet	2 Days
1941	66	F.	Duo.	Primary	Acute Massive Hem.	Starvation Diet	3 Days
1941	66	M.	?	Primary	Acute Massive Hem.	Starvation Diet	8 Hours
22 Patients	17 over 45 years of age	7 F. 15 M.	9 Duo. 8 Gast.	18 Primary 3 Secondary	1 Surgical death	2 Feeding 20 Starvation	Av. 10 Days Mean 6 Days

of 14.0 per cent. There were fifteen patients operated upon in the entire series with one death. Thus, the total surgical mortality rate was 7.0 per cent for both the acute and moderate hemorrhages.

3. Two deaths occurred in a series of seventy patients with acute massive hemorrhage treated by a prompt feeding regime. One of these patients received very little food as he entered the hospital in the

27. Browne, D. C., and McHardy, G.: Management of Peptic Ulcer Hemorrhage, *Am. J. Digest. Dis.* 6: 87, 1939.
28. Bulmer, E.: Mortality From Hematemesis, *Lancet* 2: 720, 1932.
29. Burger, G., and Hartfall, S. J.: Treatment of Peptic Ulcer Hemorrhage, *Guy's Hosp. Rep.* 84: 197, 1934.
30. Carlson, A. J.: Control of Hunger in Health and Disease, Chicago, 1939, Univ. Chicago Press.
31. Chiesman, W. F.: Mortality of Severe Hemorrhage From Peptic Ulcers, *Lancet* 2: 722, 1932.
32. Chasnoff, J., Leibowitz, S., and Schwartz, R.: An Evaluation of Meulengracht Regime in Treatment of Bleeding Peptic Ulcer, *Am. J. Digest. Dis.* 7: 373, 1940.
33. Christensen, O.: Patho-physiology of Hunger Pains, *Acta med. Scandinav.* (supplement) 37: 1, 1931.
34. Crohn, B. B., and Lerner, H. H.: Gross Hemorrhage as a Complication of Peptic Ulcer, *Am. J. Digest. Dis.* 6: 15, 1939.
35. Cullinan, E. R., and Price, R. K.: Hematemesis Following Peptic Ulcerations; Prognosis and Treatment, *St. Barth. Hosp. Rep.* 65: 185, 1932.
36. D'Alhora, J. B., and Lancellotti, W.: Bleeding Peptic Ulcer, *M. Times, New York* 66: 285, 1938.
37. Darling, H. C. R.: Surgical Treatment of Bleeding Peptic Ulcer, *M. J. Australia* 2: 167, 1940.
38. Dreys, J., and Voss, H.: Simplified Dietetic Treatment of Peptic Ulcers. *Deutsche med. Wchnschr.* 67: 292, 1941.
39. Eggeston, E. L.: A Critical Review of 500 Cases of Gastric and Duodenal Ulcer, *J. A. M. A.* 84: 1925.
40. Emery, E. S.: Comparison of Meulengracht and Sippy Therapies in Care of Bleeding Peptic Ulcers, *Am. J. Digest. Dis.* 8: 387, 1941.
41. Finsterer, Hans: Surgical Treatment of Acute Profuse Gastric Hemorrhage, *Surg., Gynec. & Obst.* 69: 291, 1939.
42. Frostad, S.: Some Statistical Data on Hematemesis and Melena, *Norsk. mag. f. Lægevidensk* 95: 578, 1934.
43. Goldman, L.: The Problem of Bleeding Peptic Ulcer, *Am. J. Surg.* 40: 545, 1938.
44. Gordon-Taylor, G.: Hematemesis, *Lancet* 1: 572, 1934.
45. Gordon-Taylor, G.: The Attitude of Surgery to Hematemesis, *Lancet* 2: 811, 1935.
46. Gordon-Taylor, G.: Problem of Bleeding Peptic Ulcer, *M. Press* 202: 313, 1939.
47. Graham, R. R.: The Surgeon's Problem of Duodenal Ulcer, *Am. J. Surg.* 40: 102, 1938.
48. Graham, J. G., Alexander, J. C., and Kerr, J. D. O.: Hemorrhage in Peptic Ulcer, *Lancet* 237: 727, 1939.
49. Gubergritz, M. M.: Treatment of Bleeding Peptic Ulcer by Diet, *Deutsche med. Wchnschr.* 62: 64, 1936.
50. Helfrich, L. S., Cassels, W. H., and Cole, W. H.: Cortical Extract in Treatment of Shock, *Am. J. Surg.* 60: 410, 1942.
51. Hellier, F. F., and Camb, M. A.: Etiology and Mortality Rate of Hematemesis, *Lancet* 227: 1271, 1934.
52. Hendon, G. A.: Treatment of Hemorrhage Caused by Peptic Ulcer, *Am. J. Digest. Dis., and Nutrition* 2: 255, 1935.
53. Herlhy, J. D.: Immediate Feeding in Hematemesis and Melena, *M. J. Australia* 2: 996, 1938.
54. Hinton, J. W.: A Review of 746 Gastric and Duodenal Ulcers, *Am. J. Digest. Dis.* 3: 59, 1939.
55. Hinton, J. W.: Massive Hemorrhage in Peptic Ulcer, *Ann. Surg.* 110: 376, 1939.
56. Holman, C. W.: Severe Hemorrhage in Gastric and Duodenal Ulcers, *Arch. Surg.* 40: 150, 1940.
57. Holman, C. W.: Treatment of Bleeding Peptic Ulcers, *Internat. Clin.* 3: 164, 1940.
58. Howard, M. C., and Barry, M. W.: Management of Hemorrhage in Duodenal Ulcer, *Nebraska M. J.* 19: 367, 1934.
59. Hurst, A. E., and Ryle, J. A.: Hemorrhage in Gastric and Duodenal Ulcers, *Lancet* 232: 1, 1937.
60. Jankelson, I. R., and Siegel, M. S.: Massive Hemorrhage From Peptic Ulcer, *New England J. Med.* 219: 3, 1938.

Seven patients with acute massive hemorrhage from peptic ulcer were operated upon with one death. Thus, the surgical mortality rate in the presence of acute hemorrhage was 14.0 per cent for a very small group of cases.

There is no proof, as yet, that those who attempt the surgical arrest of acute massive hemorrhage from a peptic ulcer are able to do so with a reasonable mortality.

REFERENCES

1. Aitken, R. S.: Treatment of Profuse Bleeding From the Stomach and Duodenum, *Lancet* 1: 839, 1934.
2. Alder, A.: Meulengracht Treatment of Bleeding Peptic Ulcer, *Schweiz. med. Wchnschr.* 69: 1286, 1939.
3. Allen, A. W.: Acute Massive Bleeding From Upper Gastrointestinal Tract, *Internat. Clin.* 4: 205, 1937.
4. Allen, A. W.: Massive Hemorrhage From Upper Gastrointestinal Tract With Special Reference to Peptic Ulcer, *SURGERY* 2: 713, 1937.
5. Allen, A. W.: Hemorrhage Associated With Ulcerating Lesions of Stomach and Duodenum, *Lahey Birthday Volume*, pp. 13, 1940.
6. Allen, A. W., and Benedict, E. B.: Acute Massive Hemorrhage From Duodenal Ulcer, *Ann. Surg.* 98: 736, 1933.
7. Alsted, G.: Diagnosis and Therapy of Peptic Ulcer, *Ugesk. f. laeger* 102: 587, 1940.
8. Andresen, A. F. R.: Treatment of Gastric Hemorrhage, *J. A. M. A.* 89: 1397, 1927.
9. Andresen, A. F. R.: Results of Treatment of Massive Gastric Hemorrhage, *Am. J. Digest. Dis.* 6: 641, 1939.
10. Balfour, D. C.: Gastro-intestinal Hemorrhage, *Surg., Gynec. & Obst.* 65: 551, 1937.
11. Balfour, D. C., and Eusterman, G.: *Stomach and Duodenum*, Philadelphia and London, 1935, W. B. Saunders Company.
12. Barnes, C. G.: Developments in Treatment of Hemorrhage From Peptic Ulcer, *Clin. J.* 68: 357, 1939.
13. Bennett, T. I., Dow, J., Lardner, F. P. C., and Wright, S.: Severe Hemorrhage From Stomach and Duodenum, *Lancet* 2: 651, 1938.
14. Bergh, G. S., Hay, L., and Trach, B.: Peptic Ulcer, *Bull. Staff Meet. Hosp. Univ. Minn.* 11: 282, 1940.
15. Bernstein, B. M.: Treatment of Bleeding Ulcer, *M. Rec.* 144: 178, 1939.
16. Bevan, A. D.: Pathological Anatomy, Etiology and Surgical Management of Peptic Ulcer, *S. Clin. North America* 14: 679, 1932.
17. Black, K. O., and Camb, M. A.: Hematemesis With Multiple Recurrences Treated With Repeated Transfusion by Continuous Drip Method, *Lancet* 2: 1430, 1937.
18. Blackford, J. M., and Cole, W. S.: Massive Hemorrhage From Peptic Ulcer—A Study Based on Vital Statistics of City of Seattle, *Am. J. Digest. Dis.* 6: 637, 1937.
19. Blackford, J. M., Smith, A. L., and Affleck, D. H.: Peptic Ulcer Emergencies, *Am. J. Digest. Dis.* 4: 646, 1937.
20. Blackford, J. M., and Williams, R. H.: Fatal Hemorrhage From Peptic Ulcer; 116 Cases Collected From Vital Statistics of Seattle, *J. A. M. A.* 115: 1774, 1940.
21. Blalock, A.: Trauma; Shock and Hemorrhage, *Bull. New York Acad. Med.* 12: 610, 1936.
22. Blalock, A.: Shock or Peripheral Circulatory Failure, *South. Surgeon* 7: 150, 1938.
23. Blalock, A.: Principles of Surgical Shock and Care, St. Louis, 1940, C. V. Mosby Company.
24. Blalock, A., and Mason, M. F.: Comparison of Effects of Heat and Cold, *Arch. Surg.* 42: 1054, 1941.
25. Bohrer, J. V.: Massive Gastric Hemorrhage; Special Reference to Peptic Ulcer, *Ann. Surg.* 114: 510, 1941.
26. Boyd, L. J., and Schlachman, M.: Meulengracht Treatment of Bleeding Peptic Ulcers, *M. Clin. North America* 22: 1397, 1938.

95. Schindler, Rudolph: *Gastroscopy*. Univ. Chicago Press, 1937.
96. Schigdt, E.: Observations on Blood Regeneration in Man. *Am. J. M. Sc.* 193: 327, 1937.
97. Scott, L. D. W.: Observations in Treatment of Severe Hematemesis and Melena, *Edinburgh M. J.* 47: 49, 1940.
98. Scudder, J.: *Shock; Blood Studies as a Guide to Therapy*, Philadelphia, Montreal, and London, 1940, J. B. Lippincott Company.
99. Segal, H. L., Scott, W. J. M., and Stevens, K. S.: Management of Gross Hemorrhage in Peptic Ulcer, *New York State J. Med.* 41: 1074, 1941.
100. Schnedorf, J. G., and Orr, T. G.: Oxygen Therapy in Shock, Due to Hemorrhage, *Surg., Gynec. & Obst.* 73: 495, 1941.
101. Shulman, N., and Glass, Frederic: Fallacious Beliefs Regarding Blood Transfusions, *J. M. Soc. New Jersey* 34: 555, 1937.
102. Snell, A. M.: The Problem of Gastro-duodenal Hemorrhage, *Minnesota Med.* 22: 15, 1939.
103. Syme, G. R. A.: Surgical Treatment of Hematemesis, *Australian & New Zealand J. Surg.* 11: 7, 1941.
104. Turnbull, G. C., and Sagi, J. H.: Bleeding Peptic Ulcer, *Am. J. Digest. Dis.* 6: 92, 1939.
105. Walters, W., and Cleveland, W. H.: Results of Partial Gastrectomy for Bleeding Duodenal, Gastric and Gastrojejunal Ulcer, *Ann. Surg.* 114: 481, 1941.
106. Westermann, J. J.: Surgical Aspects of Bleeding Gastric and Duodenal Ulcers, *Ann. Surg.* 101: 1377, 1935.
107. Wangenstein, O. H.: Problem of Surgical Arrest of Massive Hemorrhage in Duodenal Ulcer, *SURGERY* 8: 275, 1940.
108. Welch, C. S., and Yunich, A. M.: Problem for Surgery in Treatment of Massive Hemorrhage of Ulcer Origin, *Surg., Gynec. & Obst.* 70: 662, 1940.
109. Wilmer, H. A.: Blood Supply of First Part of Duodenum, *SURGERY* 9: 679, 1941.
110. Witts, L. J.: Hematemesis and Melena, *Brit. M. J.* 1: 847, 1937.
111. Woldman, E. E.: Treatment of Massive Gastro-duodenal Hemorrhage by Continuous Administration of Aluminum Hydroxide, *Am. J. Digest. Dis.* 8: 39, 1941.
112. Wood, G. O., Mason, M. F., and Blalock, A.: Effects of Inhalation of High Concentrations of Oxygen in Experimental Shock, *SURGERY* 8: 247, 1940.
113. Wood, J. J.: Treatment of Bleeding Peptic Ulcer, *Australian & New Zealand J. Surg.* 10: 363, 1941.

61. Jones, F. A.: Hematemesis and Melena; Observation on Use of Continuous Drip Transfusion, *Brit. M. J.* 1: 915, 1939.
62. Kilduffe, R. A., and DeBaKey, M.: *The Blood Bank and Technique and Therapeutics of Transfusions*, St. Louis, 1942, C. V. Mosby Company.
63. Kirsner, J. B., and Palmer, W. L.: Treatment of Massive Hemorrhage From Peptic Ulcer, *Internat. Clin.* 4: 105, 1939.
64. Kordenat, Ralph: The Relation of Blood Transfusion to Disturbance of Blood Clot Formation, *Mil. Surgeon* 66: 206, 1930.
65. Lahey, F. H.: Management of Bleeding Peptic Ulcers, *S. Clin. North America* 21: 729, 1941.
66. Lazarus, S.: Some Aspects of Treatment of Hematemesis and Melena, *Glasgow M. J.* 132: 54, 1939.
67. Lineberry, E. D., and Issos, D. N.: Treatment of Massive Hemorrhage From Duodenal or Gastric Ulcer, *South. M. J.* 30: 1228, 1937.
68. Lenhartz, H.: Treatment of Massive Hemorrhage From Peptic Ulcer, *Strantskrankenanst.* 6: 345, 1906.
69. Lynch, R.: An Analysis of Ulcer of Stomach and Duodenum, *Canad. M. A. J.* 17: 677, 1927.
70. Marriott, H. L., and Kekwich, A.: A Continuous Drip Blood Transfusion, *Lancet* 1: 977, 1935.
71. Marshall, S. B., and Kiefer, E. D.: Treatment of Acute Massive Hemorrhage in Peptic Ulcer, *Am. J. Surg.* 46: 625, 1939.
72. Mattison, K.: *Das Magenschwier*, Stockholm, 1931.
73. Mayer, W. D., and Lightbody, J. J.: Use of Food in Treatment of Bleeding Peptic Ulcers (Meulengracht Diet), *Am. J. Digest. Dis.* 6: 103, 1939.
74. Mayer, W. D., and Lightbody, J. J.: Further Observations on Use of Food in Treatment of Bleeding Peptic Ulcers, *Rev. Gastroenterol.* 8: 1, 1941.
75. McMillan, R. L.: Massive Gastric Hemorrhage From Stomach; Its Diagnosis and Treatment, *North Carolina M. J.* 2: 469, 1941.
76. Meulengracht, E.: Treatment of Hematemesis and Melena With Food, *Acta. med. Scandinav. (supplement)* 59: 375, 1934; *Lancet* 229: 1220, 1935.
77. Meulengracht, E.: The Medical Treatment of Peptic Ulcer and Its Complications, *Brit. M. J.* 2: 321, 1939.
78. Miller, T. G.: Results From Management of Bleeding Gastric and Duodenal Ulcers, *Ann. Int. Med.* 15: 390, 1941.
79. Miller, T. G., and Elsom, K. A.: Management of Massive Hemorrhage From Peptic Ulcer, *M. Clin. North America* 22: 1711, 1938.
80. Miller, T. G., and Nicholson, J. T. L.: Prompt-Feeding Program for Bleeding Peptic Ulcers, *Am. J. Digest. Dis.* 8: 446, 1941.
81. Melton, G.: Hematemesis and War, *Lancet* 1: 316, 1940.
82. Moon, H., and Lieber, M. M., and McGrew, D.: Similarities and Shock and Effects of Hemorrhage, *J. A. M. A.* 117: 2024, 1941.
83. Mossberg, O.: Prognosis and Therapy of Massive Hemorrhage in Gastric and Duodenal Ulcers, *Hygeia* 95: 898, 1933.
84. Noth, P. N., and Wilbur, D. L.: Diagnosis and Treatment of Gastro-intestinal Hemorrhage, *Proc. Staff Meet., Mayo Clin.* 10: 824, 1935.
85. Paterson, H. J.: Treatment of Severe Gastric and Duodenal Hemorrhage, *Proc. Roy. Soc. Med.* 17: 2, 1932.
86. Pfeiffer, D. B.: Gastric Hemorrhage, *J. A. M. A.* 111: 2198, 1938.
87. Polayes, S. H., and Morrison, M.: A Study of the Results of 1,500 Transfusions in 1,000 Cases, *Am. J. M. Sc.* 184: 326, 1932.
88. Rafsky, H. A., and Weingarten, M.: Bleeding Peptic Ulcer; Treatment Based on Series of 408 Cases, *J. A. M. A.* 118: 5, 1942.
89. Rankin, F. W., Johnston, C., and Coleman, C.: Bleeding Peptic Ulcer—Indications for Surgery, *South. Surgeon* 8: 298, 1939.
90. Reschke, K.: Die Behandlung schwerster Blutungen bei der Magengeschwürskrankheit, *Deutsche med. Wchnschr.* 61: 1268, 1935.
91. Reschel, A.: Further Observations of Treatment of Hematemesis and Melena With Meulengracht Diet, *Acta. med. Scandinav. (supplement)* 78: 418, 1936.
92. Rivers, A. B., and Wilbur, D. L.: Intrinsic Gastro-duodenal Lesions as Causative Factor of Hematemesis, *Arch. Int. Med.* 50: 621, 1932.
93. Ross, K.: Treatment of Hemorrhage From Peptic Ulcers, *M. J. Australia* 1: 168, 1930.
94. Schiff, J.: Medical Treatment of Bleeding Peptic Ulcer, *J. Med.* 21: 437, 1941.

he has noticed no attributable reduction in mortality. When mechanical obstruction of a strangulating character is known to be present, he advises against sole reliance on the tube; whereas it might be more safely put that one should depend solely on the tube only when it is known that mechanical obstruction is not present. The differentiation of the types of obstruction is didactic and oversimplified.

This reviewer is grateful for Dr. Wangenstein's attack on two time-honored surgical maxims repeated from text to text and lecture to lecture. He maintains, with good reason, that in acute appendicitis with peritonitis death is not due to paralytic ileus but to infection. The old dictum that high intestinal obstruction is more lethal than low is shown to date from the period before adequate fluid replacement. A patient with high obstruction can be carried along, with replacement of fluids, long after a patient with low small intestinal obstruction has succumbed to the effects of distention and pressure in a long stretch of bowel.

Many of the sections on special types of obstruction are interesting. It is a little hard to understand the frequent reference to obstruction of the intestine by gallstones.

The use of enterostomy in surgical management of intestinal obstruction is very strongly stressed and recommended, an attitude which is at variance with present-day surgical practice in most clinics.

Epilepsy and Cerebral Localization. By Wilder Penfield, M.D., D.Sc., and T. C. Erickson, M.D., M.A., M.Sc., McGill University. Pp. 623, with 163 illustrations. Charles C Thomas, Publisher. Springfield, Ill., 1941. \$8.00.

This well-written, encyclopedic treatise on epilepsy contains material from the authors, many contributions concerning epilepsy published in the periodic literature, and, in addition, a most comprehensive review of the literature on epilepsy. Focal epilepsy is the type which the authors have most extensively investigated, but all types of epilepsy are fully discussed in this book.

Since the investigation of the mechanism and treatment of focal epilepsy has led the authors to extensive study of cerebral localization, it is natural that the whole subject of functional localization in the cerebral cortex, its history and present status should be reviewed here. They have had the most extensive experience with observations in stimulation of the cerebral cortex of conscious patients.

This book is a most comprehensive treatise on the history, mechanism, etiology, surgical treatment, medical treatment, and psychology of the epileptic patient.

An abundance of illustrative case reports are given in detail. The efficient arrangement which the authors have for taking photographs in the operating room is reflected in the many photographs of exposed cortex. However, the diagrams which supplement these photographs are equally, if not more, helpful to the reader.

The large amount of original investigation reported and the laborious compilation and inclusion of information from the literature should make this book one of lasting value.

Synopsis of Pathology. By W. A. D. Anderson, M.A., M.D., Pp. 661, with 294 illustrations, and 17 color plates. St. Louis, 1942, C. V. Mosby Company.

This book is one of a recent series of synopsis of various subjects related to the study of medicine. The value of any one of these condensed presentations will depend upon two main points, namely: (1) the completeness with which the author has covered the subject to include the various phases of the subject under discussion and (2) the brevity with which each phase is presented.

Book Reviews

History and Evolution of Surgical Instruments. By C. J. S. Thompson, Royal College of Surgery, London, with a foreword by Chauncey D. Leake. Pp. 113, illustrations 115, New York, N. Y., 1942. Schuman's.

Professor Thompson, a well-known English medical historian, sets forth in this monograph a brief recital of what is known concerning the development of surgical instruments. The monograph is particularly valuable now, in that the author has surveyed the fine collection of surgical instruments which, before the Nazi aerial bombardments of London, contributed one of the most remarkable historical collections of surgical instruments extant. That collection has now been largely destroyed. It is particularly fortunate, therefore, that this survey of the author was well under way before that grim act of destruction occurred.

It is interesting to observe in this monograph the development of various instruments. Those instruments like the saw used by cabinetmakers still were well developed 100 years and more ago, resembling very closely those used by modern surgeons; similarly, the instruments used for trepanation of the skull, having as antecedents the brace and drill of the cabinetmaker, early assumed a form not unlike that of modern instruments used for the same purpose. When the surgeon had to do his own improvising, it is painful to observe how slow his progress was as witness the slow development of the artery forceps and instruments for dissection. The story of the development of the scalpel and the operating table reflects quite directly the role of the surgeon's activity. Prior to anesthesia and aseptic surgical practices, the point of the scalpel received the greatest notice from surgical innovators; thereafter, the blade poised for cutting became the chief object of concern. The author concludes with the suggestion that more recent developments in the facilities of the surgeon in the operating room "are a story in themselves"—a chapter with which he does not wish to deal.

The book is one which should interest all surgeons, with a historical sense, who desire to know something of the manner in which his instrumentarium came into being.

Intestinal Obstructions: A Physiological and Clinical Consideration with Emphasis on Therapy; Including Description of Operative Procedures. By Owen H. Wangensteen, B.A., M.D., Ph.D., Professor of Surgery of the University of Minnesota and Surgeon-in-Chief of the University of Minnesota Hospital, Minneapolis. Ed. 2. Cloth. Pp. 484, with 143 illustrations, of which 82 are newly introduced in this edition. Springfield, Ill., 1942, Charles C Thomas, Publisher. \$7.00.

The second edition of Dr. Wangensteen's book, which is considerably larger than the first, remains a useful monograph and compendium of information on intestinal obstruction. The author's own important contributions to the subject are many.

The discussion of the pathologic physiology of intestinal obstruction, with particular stress on the author's "mechanistic" interpretation, is excellent. References are plentiful, well chosen, and separately grouped after each chapter.

The use of indwelling tubes is fully discussed. The author permits himself to say that while he has abandoned the duodenal tube for the Miller-Abbott tube,

he has noticed no attributable reduction in mortality. When mechanical obstruction of a strangulating character is known to be present, he advises against sole reliance on the tube; whereas it might be more safely put that one should depend solely on the tube only when it is known that mechanical obstruction is not present. The differentiation of the types of obstruction is didactic and oversimplified.

This reviewer is grateful for Dr. Wungensteen's attack on two time-honored surgical maxims repeated from text to text and lecture to lecture. He maintains, with good reason, that in acute appendicitis with peritonitis death is not due to paralytic ileus but to infection. The old dictum that high intestinal obstruction is more lethal than low is shown to date from the period before adequate fluid replacement. A patient with high obstruction can be carried along, with replacement of fluids, long after a patient with low small intestinal obstruction has succumbed to the effects of distention and pressure in a long stretch of bowel.

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Dr. Anderson presents a condensed discussion of the pathologic changes occurring in disease, as well as a discussion of the pathologic processes occurring in these same diseases as related to their application to clinical medicine. The very nature and purpose of this book precludes the possibility of completeness of discussion in any of the subjects presented. However, for the most part, the author has not, apparently, sacrificed clarity of description for brevity of presentation.

The descriptions and discussions are supplemented by a wealth of black and white photographic plates of the gross as well as the microscopic changes occurring in the different parts of the body. With a few exceptions, the detail of these photographs is excellent and because of this they greatly augment the value of the brief descriptions to which they refer. In addition to the innumerable photographs mentioned, there are seventeen color plates.

As mentioned in the preface, the bibliography is very incomplete. Unfortunately, this is unavoidable in such a condensation of so vast a subject. However, the references, which are listed, are of recent date and should form a basis for further investigation of any subject discussed.

Textbook of Surgery. By American authors, edited by Frederick Christopher, BS, MD, F.A.C.S. Ed. 3. Pp 1764, with 1538 illustrations on 771 figures. Philadelphia and London, 1942, W B Saunders Company. \$10.00

The first edition appeared in 1936 and, as the editor states, "The dominant plan of this textbook is to give the student a concise presentation of surgery which is characterized by the maximum authority. The contributors, whose painstaking work has made this book possible, have been chosen because of their outstanding ability in the subjects which they present. The subject matter contains the tested and accepted present day principles of surgery. Etiology, pathology, and diagnosis have properly been stressed, and the correct surgical treatment has been carefully described." A second edition was published in 1939.

The present publication is an up to date, practical treatise on surgery which follows the design of previous editions. There are several new sections, including one on war injuries, pruritus and hemorrhoids, abnormalities of the thymus, compound fractures, coccidioidal granuloma, and patent ductus arteriosus. Other sections have been completely revised or rewritten. The utilization of a great number of collaborators, writing upon the field of their special interests, is the distinctive feature of this volume, consequently, it carries the advantage of more authoritative and precise information than texts of different plan and format. Throughout the text, various contributors have indicated the many applications of the sulfonamide group of drugs and the beneficial results which may be expected. Pertinent references to literature are appended at the end of each discussion for readers who wish to study the subject more extensively.

This book is generally eminently practical, it is fundamental enough for students and is not too brief as a reference book for practitioners. There is little that one can criticize. The illustrations, both diagrams and photographs, are well chosen. As is so often the case, there is no lack of definitive information concerning the mortality as well as the results of surgical intervention.

To all physicians engaged in the practice of surgery this valuable book is seriously and enthusiastically recommended.

It is with deep regret that we announce the death of Doctor Charles Virgil Mosby, chairman of the board of The C. V. Mosby Company, St. Louis, Mo., on November 9, 1942.

His vision and courage will continue as an inspiration throughout the future of the company that he founded.

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Dr. Anderson presents a condensed discussion of the pathologic changes occurring in disease, as well as a discussion of the pathologic processes occurring in these same diseases as related to their application to clinical medicine. The very nature and purpose of this book precludes the possibility of completeness of discussion in any of the subjects presented. However, for the most part, the author has not, apparently, sacrificed clarity of description for brevity of presentation.

The descriptions and discussions are supplemented by a wealth of black and white photographic plates of the gross as well as the microscopic changes occurring in the different parts of the body. With a few exceptions, the detail of these photographs is excellent and because of this they greatly augment the value of the brief descriptions to which they refer. In addition to the innumerable photographs mentioned, there are seventeen color plates.

As mentioned in the preface, the bibliography is very incomplete. Unfortunately, this is unavoidable in such a condensation of so vast a subject. However, the references, which are listed, are of recent date and should form a basis for further investigation of any subject discussed.

Textbook of Surgery. By American authors, edited by Frederick Christopher, B.S., M.D., F.A.C.S. Ed. 3. Pp. 1764, with 1538 illustrations on 771 figures. Philadelphia and London, 1942, W. B. Saunders Company. \$10.00.

The first edition appeared in 1936 and, as the editor states, "The dominant plan of this textbook is to give the student a concise presentation of surgery which is characterized by the maximum authority. The contributors, whose painstaking work has made this book possible, have been chosen because of their outstanding ability in the subjects which they present. The subject matter contains the tested and accepted present-day principles of surgery. Etiology, pathology, and diagnosis have properly been stressed, and the correct surgical treatment has been carefully described." A second edition was published in 1939.

The present publication is an up-to-date, practical treatise on surgery which follows the design of previous editions. There are several new sections, including one on war injuries, pruritus and hemorrhoids, abnormalities of the thymus, compound fractures, coccidioidal granuloma, and patent ductus arteriosus. Other sections have been completely revised or rewritten. The utilization of a great number of collaborators, writing upon the field of their special interests, is the distinctive feature of this volume; consequently, it carries the advantage of more authoritative and precise information than texts of different plan and format. Throughout the text, various contributors have indicated the many applications of the sulfonamide group of drugs and the beneficial results which may be expected. Pertinent references to literature are appended at the end of each discussion for readers who wish to study the subject more extensively.

This book is generally eminently practical, it is fundamental enough for students and is not too brief as a reference book for practitioners. There is little that one can criticize. The illustrations, both diagrams and photographs, are well chosen. As is so often the case, there is no lack of definitive information concerning the mortality as well as the results of surgical intervention.

To all physicians engaged in the practice of surgery this valuable book is seriously and enthusiastically recommended.

It is with deep regret that we announce the death of Doctor Charles Virgil Mosby, chairman of the board of The C. V. Mosby Company, St. Louis, Mo., on November 9, 1942.

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